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T H E S I S

Presented for the Degree of Doctor of Medicine

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on

CONSECUTIVE TESTS, by the FRACTIONAL METHOD of GASTRIC ANALYSIS, in Seventy-five Cases presenting GASTRIC SYMPTOMS.

BY

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I N D E X.

VOLUME I.

I N T R O D U C T I O N.

The Fractional Method of Gastric Analysis may be said to have been established in this country and in America by the work of REHFUSS[1] in the year 1914.

Nearly eight years later, KOPELOFF[2] wrote as follows:-

> "In a review of the literature on this method (The Fractional Method of Gastric Analysis) and its application, a surprising fact was noted. So far as could be determined there has been published no series of fractional analyses on the same individual at different times, using the same test meal, and having all other physical and mental conditions as nearly identical as possible. The necessity of performing such experiments in order to establish the errors inherent in the method is apparent, yet neither the literature, nor private correspondence has revealed such information".

KOPELOFF[2] supports this observation by a very exhaustive list of references to fractional analysis/

analysis, available up till the year 1922. These remarks introduce a paper upon the results of his investigations into consecutive test meals, performed at short intervals in twenty persons suffering from "so-called functional psychoses" but presenting no gastric symptoms, and in ten healthy nurses.

At about the same time BENNETT & RYLE (3), published the results following their investigation of one hundred healthy male students by this fractional method. In the same publication they record that they "have carried out a considerable number of controls", to ascertain the extent of daily variations in respect to fractional analysis.

They give the conclusions they have drawn from these control experiments but nowhere record the number of experiments performed, or any data in support of their statements.

In 1924 BELL & McADAM (4), wrote:-

"The only references we have been able to discover with regard to daily variations in the acid curves of a normal individual are contradictory. LYON, BARTLE & ELLINSON (5), in remarking on the variations in the acid values

in/

in different normal persons, say ' if the stomach contents of the same individual are examined daily under the same conditions of time, and length of preceding fast, great variations of acid value will frequently be seen'".

They then record the observation made by BENNETT & RYLE (3), in this connection to which I have referred already, but apparently they did not refer to KOPELOFF'S (2) work upon this subject.

They add their own contribution to a controversial subject in the form of an investigation of one healthy male by fractional gastric analysis upon twenty consecutive days.

I would record here that reference to the original paper by LYON, BARTLE & ELLINSON (5), shows that the remarks abstracted from this paper by BELL & McADAM refers to variations in the acid values in the resting and unstimulated stomach, and, therefore, these remarks cannot be applied to variations following a "fractional test meal".

More recently RYLE (6), has recorded the results of repeated fractional analysis in one case. (RYLE himself).

This/

This concludes the entire list of references which I have been able to find, bearing on the study of possible daily variations in the results obtained from the fractional method of gastric analysis.

It will be seen that apparently a limited number of persons have been examined from this point of view:-

(1) Twenty persons suffering from "so-called functional psychoses". (KOPELOFF).

(2) Ten healthy nurses. (KOPELOFF).

(3) "A considerable number" of healthy male students. (BENNETT & RYLE).

(4) One healthy male. (BELL & McADAM).

(5) One healthy male. (RYLE).

Even were these observers in agreement, the limited number of cases investigated would make it questionable whether daily variations in acid curves had been studied adequately. But the fact that the conclusions drawn by these workers are contradictory makes further investigation almost imperative.

KOPELOFF'S (2) conclusions are brief, but emphatic. He writes. "Subject to the limitations of the investigation (thirty cases) it is indicated that/

that single determinations of gastric acidity by the REHFUSS method are not sufficient on which to base conclusions because they do not take into consideration individual variations".

BENNETT & RYLE (3), under the heading of Variations from Day to Day in the Curve of a Given Subject write. "We have carried out a considerable number of controls to ascertain the extent of this variation. No experiment could better demonstrate the value of the fractional method; in several instances exactly identical curves have been obtained when taken on different occasions. In general it has been found that slight differences may be found towards the end of the curve, corresponding with the amount of duodenal regurgitation at a particular moment, this regurgitation, due to the tonus of the pylorus, which changes momentarily, must evidently be a variable factor from day to day, and from meal to meal".

BELL & McADAM (4), summarised the result of their investigation of one man by "standard deviations and coefficient of variations of the acidities of different/

different specimens at corresponding times".

Generally speaking they found that variations between daily curves were slight, but that the curve obtained on the occasion of the first test was definitely lower than those obtained from the subsequent tests.

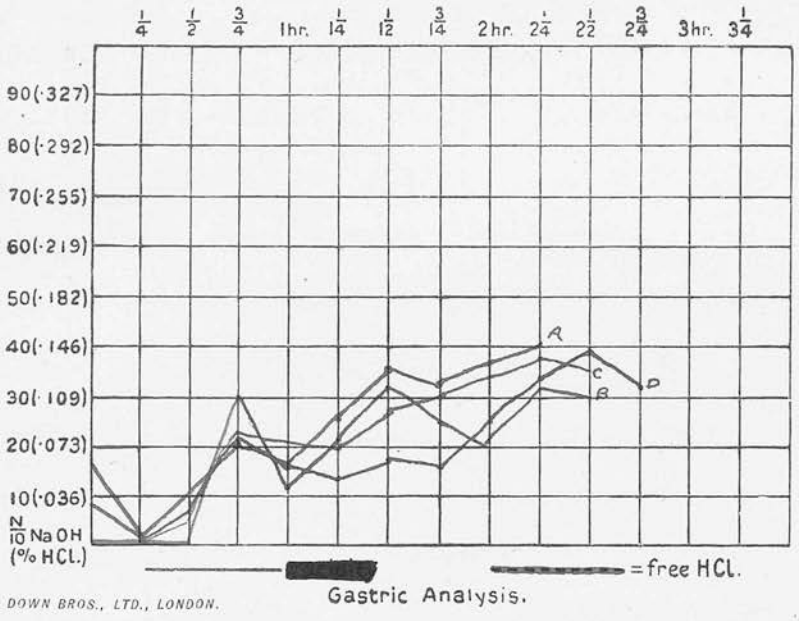
RYLE (6), as recently as January 1926 writes as follows:-

"It is important to dispose of the criticism that the variations in the responses of the same individual from day to day may be so wide as to invalidate the test. On the analogy of the variable tonic and peristaltic behaviour of the stomach, secretory variations would also be anticipated, and such changing factors as appetite and hunger varying rates of neutralisation and minor differences in the conditions of the test might be expected to find reflections in the acid curves.

We do not expect constant behaviour on the part of other glands such as the salivary and sweat glands even under closely parallel conditions.

With/

CHART A.



Showing response of same individual on four different occasions.

Standard gruel meal;

(a) 18/1/20.
(b) 25/1/20.
(c) 1/2/20.
(d) 9/5/20

The curves are those of free acidity.

[Ryle].

With the fractional test meal the conditions are, so far as possible standardised by carrying out the test at the same time in the morning after the nights rest, by employing the same meal and the same method, and by encouraging the subject to occupy his or her mind with a book or other diversion during the period of the experiment.

With these precautions the variation in the results obtained from the same individual on different dates have generally been slight.

Where they appear more considerable the general conformation of the curve is maintained and the rate of emptying is very constant.

Subjects with low curves or achlorhydria show low curves achlorhydria; subjects with high curves show high curves on subsequent occasions. The four curves of free acidity shown in chart A were obtained, in my own case, on the dates indicated.

BELL & McADAM (4), performed the experiment of examining the same man on no less than twenty consecutive days. They found the rate of emptying/

emptying remarkably constant. On thirteen occasions it was one and a half hours. On five occasions it was one and three quarter hours; on two occasions it was two hours.

The general conformation of the curve obtained on the first day was distinctly lower than on any subsequent day".

I have quoted this section of RYLE'S book in full, to show how flimsy is the foundation of the answer, which can be given even to-day, to the criticism that daily variations invalidate the results obtained by the fractional method of gastric analysis.

It is noteworthy, too, that RYLE does not refer to the findings of KOPELOFF (2), in this connection, though on the page which follows the section of his book which I have quoted he writes:-

"KOPELOFF examined ten young pupil nurses each on several occasions".

He goes on to show that he has examined KOPELOFF'S results, but refers ti them only as being comparable to the results obtained in his own series of normal males, and nowhere records KOPELOFF'S findings in regard to daily variations as the result of consecutive/

consecutive analysis in these ten nurses.

This ommision becomes significant when it is recalled that KOPELOFF concludes that "single determination of gastric acidity by the REHFUSS method are not sufficient on which to base conclusions".

It suggests that the fractionak method of gastric analysis is not, at the present time, in a position to face criticism of this nature.

Further it is noteworthy that all such investigations as have been carried out with a view to studying possible daily variations have been performed in normal persons. I have found no record of any study of possible daily variations in persons presenting gastric symptoms; such persons, in fact, as will be examined clinically by this test, and for whom the test is intended.

I have been able under circumstances which I shall now record briefly, to examine personally by the fractional method of gastric analysis on two or more occasions seventy five persons, all presenting gastric symptoms.

The consecutive tests were performed at short/

short intervals of time, and under circumstances as nearly as possible identical on each occasion.

I had not long undertaken my duties as House Physian to Chalmers Hospital before I realised that, in the course of my work, I should be called upon to examine many cases by the fractional method of gastric analysis.

It seemed to me that several features of this test were still sub judice. I determined, if it were possible, to make some investigation of the test, such as might be conducted in conjunction with and yet supplementary to, my routine work.

It was realised at once that with the few beds at my disposal, and my relatively short tenure of office, it would be impossible to undertake the investigation of any very extensive series of cases.

Actually twenty beds only have been available, and the investigation has been carried out during the six months from October last which has been the duration of my present appointment to this hospital.

Since these twenty beds have been open for medical cases of all kinds, no special selection of gastric/

gastric cases could be made.

It has proved fortunate, however, from the point of view of my investigation that cases presenting gastric symptoms form such a large proportion of general medical patients. With these few beds to draw upon, and in this short space of time I have been able to investigate seventy five cases.

The arrangements in this hospital for the reception of patients are unique, and, therefore, it is desirable to give an outline of the following points.

The Hospital is divided into two sections, relative to the admission of patients. These sections are termed for convenience (1) "Private" and (2) "Public" wards. Patients admitted to the former pay half a guinea per diem for board, but no other fees of any kind are charged, except a nominal fee for X-ray examination.

The patients admitted to the public ward pay absolutely nothing, and are, therefore, on the same basis as patients admitted to any large voluntary teaching hospital.

There are male and female beds, in about equal number, in the two sections of the Hospital.

No/

No teaching of medical students is carried out in this hospital.

The type of case, therefore, in my series varies considerably from the usual run of hospital patients, accordingly there has been a wider field to sample than is usually possible in work of this kind.

A small part of the dispensary of the hospital is equipped for carrying out the usual routine tests connected with diagnosis, but there is no elaborate equipment of any kind such as one is accustomed to find in any modern laboratory for clinical research.

Every test has been carried out by me within this hospital, and all the samples have been examined by me in this dispensary. Therefore, there is this advantage that any error in reading the colour changes, or titration end points, should be perpetuated in the same percentage, and should be, therefore, strictly comparable in all cases.

Practically all the testing was carried out under similar conditions of lighting.

In all cases presenting gastric symptoms Dr. Hewat, physician to the hospital and my chief, expected/

expected a routine "test meal" examination to be carried out. The primary object in carrying out test meal examination was from the point of view of gaining a factor in the culumative evidence on which to base a clinical diagnosis in each case, and my duties have made this view point in regard to the tests necessarily of primary importance in my estimation.

Since no reference, however, could be found to consecutive test meals in "patients", it was simple though laborious to expand the routine examination to include a second, or even third test meal.

This part of the investigation might rightly be considered as devoted to "spare time", and it is this "spare time" investigation which has formed the structure of this thesis.

Throughout the course of the investigation I endeavoured to consult as much of the literature on fractional test meals as possible, and literature upon this subject has become extensive.

Research in this respect showed that misquotation is not infrequent, and for this reason the labour of this section of the work was increased, because original articles and papers required to be consulted in full.

Since/

Since in principle this test depends upon Physiological conceptions I have endeavoured to acquaint myself with the most recent advances in the field of Gastric Physiology, and I have devoted a few pages of my thesis to this aspect of my work.

In another short section the comparative merits of various gastric secretory and gastric motility tests are discussed.

I should also like to add that the interest which my chief Dr. Hewat, has shown in this work has been an inspiration in itself.

To Mr. Dowden I am indebted for the kindly interest he has taken in elucidating various points in those patients who came to operation.

Mr. Dott has given me material assistance with the recent literature of the subject, and I am indebted to Mr, D.M. Greig for certain original papers which he was able to obtain for me.

To these gentlemen, and to Miss Crawford and Dr. Henderson, who have given valuable assistance in the preparation of certain diagrams and illustrative charts, I wish to express my gratitude.

In/

In summary then, I submit in this thesis, an investigation into the variations which exist in the results obtained from consecutive "fractional test meals" in persons presenting gastric symptoms.

So far as I can ascertain , such an investigation has not been attempted previously.

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4. BELL & MACADAM, Quart. Journ. Med. xvii, 1924

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THE PHYSIOLOGY of the STOMACH.

Gastric physiology covers such a wide field that it would be manifestly impossible to include more than a brief outline of some of its more important features, in a thesis such as this.

In recent years a great deal of work has been directed towards this subject, and a mass of data relative to small fragments of the problem has been accumulating. But, in spite of the advances which have been made, we are still without any clear cur picture of many of the phenomena concerned, and much recent work has, in many cases, only served to throw into disrepute facts, which for many years were held to be definitely established.

In studying this subject, I have been influenced largely by my interest in fractional test meals, and any recent work which seemed to have a bearing upon this test, has received special consideration; and, in so far as I have been able, I have considered all the information published up to the end of 1925, which has been available.

Special attention has been paid to the work of CARLSON, and his co-workers in Chicago, partly because of the special interest they have developed in this section of physiology, and partly, because of/

of the desire they show to correlate their findings with clinical phenomena.

I have divided the subject into three Sections:-

I. GASTRIC SECRETION.

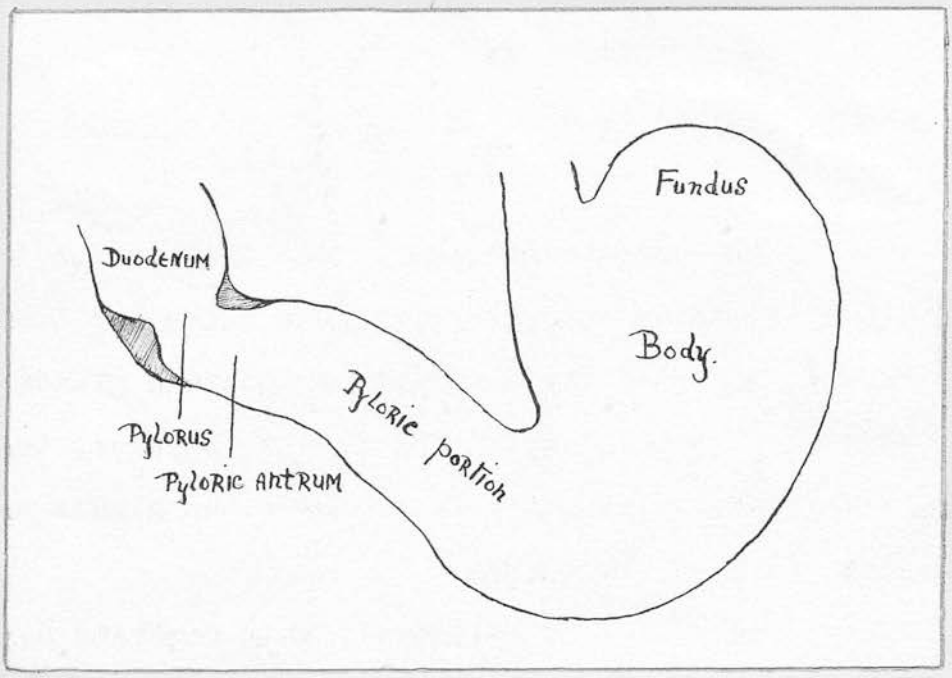
II. GASTRIC MOTILITY.

III. NERVOUS MECHANISM,

and these will be dealt with in that order.

I./

FIG. I.



Schematic diagram of regions of the stomach, showing the application of the terminology used in thesis in this connection.

[Gray's Anatomy].

I. GASTRIC SECRETION.

THE GASTRIC MUCOSA & SECRETING CELLS.

The mucous membrane lining the stomach is a relatively thick one, the thickness being due largely to the length of the long tubular gastric glands, (SCHÄFER)[1]. At the dome of the fundus, however, the membrane becomes thinned out, and here the glands are found to be fewer in number.

This area of relatively thin membrane seems to correspond to the "air-cap" described by radiologists; and LIM[2] has suggested, that the presence of a thinner membrane, and fewer glands in this part of the stomach, is explicable on the absence of contact with food. The surface epithelium consists of columnar goblet cells, which are mucus secreting in function. It is undetermined whether or no these cells play any part in modifying gastric juice, by absorption or diffusion: that such a possibility requires further investigation is suggested by BENNETT[3], recording that he has been greatly impressed by the apparent capacity for adsorption which gastric mucus possesses.

The glands are simple tubules, except in the/

the region of the pyloric antrum and the cardiac orifice, where they become tubulo-racemose in character. There are three types of cells found in relation to these glands.

HEIDENHAIN (4), described only two types, named parietal and central, according to their relationship to the lumen of the gland.

The parietal type of HEIDENHAIN, are the oxyntic, or acid secreting cells, and these are found in all the glands of the stomach, except in the region of the pyloric antrum, where acid secreting cells are few in number, or absent entirely.

The central type of HEIDENHAIN have been still further differentiated by BENSLEY (5), into superficial or neck cells, and deep cells, named according to the position they occupy in the gland in reference to the lumen of the stomach.

These neck cells, though they preponderate at the neck of the glands lying in the body of thestomach, are found freqeuntly extending throughtout the greater part of these glands, and they are identical with the cells forming the glands in the pyloric and cardiac regions of the stomach, where oxyntic cells are hardly in evidence. LIM (6). The staining reaction/

reaction of these superficial cells is similar to that of mucus secreting cells, and BENSLEY has suggested, that their sole function is the secretion of mucus. LIM & DOTT (7), however, have found a feeble proteolytic enzyme in secretion from a pyloric antrum which showed histologically, the presence of superficial cells only.

The deep cells of BENSLEY have all the characteristics of zymogen secreting cells, and are responsible for the pepsin of gastric juice. The distribution of these cells appears to be similar to that of the oxyntic cells, but smaller in extent.

THE NATURE of GASTRIC SECRETION.

Gastric secretion is a continuous process, and it may be said in general, that the stomach never stops secreting. This statement is contrary to the view held by PAVLOV (8), that gastric secretion was an intermittent process, requiring stimulation by food, or psychic factors, before secretion was produced normally.

CARLSON (9), working on cases of gastric fistula, and other observers, KUNDE (10), have shown, however, that there is an incessant flow of juice in the empty/

empty, and apparently resting stomach, and this occurs in the absence of all recognisable stimuli.

Further CARLSON has shown that secretion continues even after prolonged fasting, and states that the continuous secretion is usually not uniform in rate, but the periodicity of this secretion is less marked than the periodicity of the motor phenomena of the empty stomach. (vide infra)

This juice secreted in the apparently unstimulated stomach, is true gastric juice BRESKIN & BYKOFF (11); but as contrasted with the copious, watery, strongly acid, and highly proteolytic juice which follows stimulation, it is usually scanty and viscid, with a variable amount of free HCl, but always some total acid and ferment.

Several observers BERGHEIM (12), LIM (13), have shown that the secretion of HCl is apparently indefatigable; but LIM (14), states there is reason to believe, that pepsin formation cannot go on indifinitely, a period of rest being required for the peptic cells to elaborate the zymogen precursor, so that though acid secretion in the continuous juice may cease spontaneously, while pepsin secretion is normally continuous, yet even in a stomach which is excessively/

excessively stimulated, there will be no fatigue of acid secretion, while it is suspected that pepsin would show a marked diminution.

COMPOSITION of GASTRIC JUICE.

The contents of the stomach removed by aspiration through a stomach tube, cannot be taken to represent a true picture of normal gastric secretion, for in using such a method there is no control over the contamination of the stomach contents by saliva, or by regurgitation of the duodenal juice.

Pure gastric juice can, however, be obtained from fistulae & pouches in dogs, and from fistulae cases in man; an additional method of obtaining relatively pure juice in normal man is that devised by LIM, MATHESON and SCHLAPP (15), which consists of combined stomach and duodenal intubation, along with continual suction applied to both tubes.

Pure gastric juice, obtained by any of the above methods, has been found to contain HCl, pepsin, rennin, lipase, mucus, and various salts.

In addition to these more generally recognised constituents LOEFER & MARCHAL (16), have found that leucocytes constantly pass into the gastric juice and/

and may do so during psychic secretion.

With regard to the percentage composition of pure gastric juice most observers are in essential agreement. The only figures which will be quoted as bearing on the present thesis are those for acidity:-

Free HCl = 0.40 - 0.50%

Total Acidity = 0.45 - 0.60%

no higher figure than 0.60% having been observed to occur. The importance of this point will be dealt with later in considering the clinical condition of hyperacidity.

THE DIFFERENCE BETWEEN CONTINUOUS and STIMULATED SECRETION.

From the fact that continuous secretion is usually not uniform in rate, and that CARLSON (17), found in his fistula cases, different rates of secretion in the same individual on different days, it is clear that continuous secretion is not invariably a minimal secretion. So that it is not inconceivable that stimulated secretion may be continuous secretion in an enhanced form.

Using the amount of HCl secreted per unit of time, as a measure of the secretion rate, LIM (18), has/

has shown that the volume of juice secreted, both under continuous and stimulated conditions, increases proportionately with the secretion rate, and that the percentage acidity increases with the ratio of secretion rate to volume.

The difference in character between continuous and active secretion is, therefore, quantitative rather than qualitative, as regards HCl, the chief difference being the greater increase in the amount of juice secreted under stimulated conditions.

With reference to the pepsin content it is only known that under stimulated conditions its amount increases along with that of the acid. LIM finds it probable that irregular fluctuations in the percentage acidity of gastric juice are due to variations in the amount of non-acid bearing juice, and this implies that the HCl is secreted by the cells at a constant concentration.

RELATION BETWEEN STIMULUS and RESPONSE.

It does not matter in what way the stomach is stimulated, the response broadly speaking, remains the same, for any stimulus calls forth a simultaneous increase of juice, acidity and ferment.

As a result of his investigations PAVLOV (19), came to the conclusion that there was a qualitative adaptation in a gastric secretory response, according to the qualitative differences in the stimuli (food) at work, and he defines broad differences between "meat juice", "bread juice", and "milk juice".

Reviewing this subject in 1923 CARLSON (20), criticised the data supporting this view as inconclusive, and stated this qualitative adaptation required reinvestigation in the light of more recent knowledge. He suggested that alterations in acidity and pepsin concentration, in relation to the secretory rate, might be sufficient to explain the qualitative differences between "meat" and "bread juice".

More recently LIM (21), has shown that a constant stimulus calls forth a tolerably constant response of HCl, and that when the responses to different/

different stimuli are referred to the secretory rate, the difference between these responses is due mainly to the difference in the intensity of the secretion, and therefore to the strength of the respective stimuli, though, of course, the quantity and concentration of the response will be found to differ with the different stimuli.

The importance of this question lies in the fact that PAVLOV'S view requires a relative independancy of secretory process for the different constituents of gastric juice, and either a specific sensibility of the afferent paths of the secretory mechanism, or a different secretagogue factor in the different foods. Such factor would add greatly to the complexity of the gastric mechanism, as at present we imagine it to be.

SITES of STIMULATION.

In addition to the obvious site, namely local stimulation of the stomach itself, there are several other sources from which stimulation may arise.

PAVLOV (22), was the first to demonstrate that certain stimulations, applied direct to the duodenum/

duodenum, might produce gastric secretion.

More recently IVY, LIM, & Mc CARTHY (23), have given additional importance to the intestine as a site of gastric stimulation, and have shown that many substances known to be present in the intestines after a meal, may produce gastric secretion.

PAVLOV (24), again was the first to demonstrate gastric secretion produced by psychic factors, through taste, sight and smell of food.

Further LUCKHARDT & JOHNSTON (25), have shown that suitable hypnotic suggestion will produce gastric secretion, and JOHNSTON & WASHEIM (26), report that the state of hypnosis itself, and, probably normal sleep have a stimulating effect upon secretion.

WEITZ & FISCHER (27), find that a cold bath is a definite stimulus to gastric secretion.

EFFECTIVE STIMULI.

With reference to effective stimuli to psychic secretion little need be said.

Seeing, smelling, and tasting food, when the state of hunger or appetite is present, are effective stimuli to secretion in man; of these, taste appears to be the most potent. Apparently the/

the act of chewing in itself - using substances unrelated to food for this purpose - does not stimulate secretion (CARLSON [20]), In addition to the increased secretion caused by the state of hypnosis itself (JOHNSTON & WASHEIM [26]), suggestions of hunger, food, and eating, are effective stimuli while in the hypnotic state (LUCKHARDT & JOHNSTON [25]),

Earlier observers, influenced by BEAUMONT'S [28], work on his gastric fistula case (Alexis St. Martin), generally held the view that mechanical stimulation was the effective factor in the production of secretion from local stimulation of the stomach itself. But as the result of PAVLOV'S [24], experiments, this view became discredited, and it was generally thought that secretion was produced through chemical factors.

More recently LIM, IVY & Mc CARTHY [29], have shown that mechanical distension of the stomach stimulates secretion in man and in dogs, (in the latter under circumstances eliminating all possibility of psychic secretion). This discovery necessitated a repetition of many of the earlier experiments on chemical stimulation, in which the quantities (food) used were sufficient to cause mechanical/

mechanical distension

The repetition experiments have given results which still substantiate PAVLOV'S observations on specific chemical stimulation.

The inadequacy of mechanical stimulation, by such means as glass rods, sand blasts etc., observed by PAVLOV remains undisputed, so that chemical stimulation and mechanical distension have both been shown to be effective stimuli of gastric secretion when applied locally.

As a result of their work on gastric secretion produced by stimulation of the intestine, IVY, LIM & Mc CARTHY (30), find that chemical stimuli only are effective.

MECHANISM of SECRETION

The mechanism of continuous gastric secretion is quite unknown. That it is not a phase of the normal stimulation arising from products of digestion in the intestine, as suggested by IVY, Mc ILVAINE (31), and JAVOIS (32), is shown by the fact that continuous secretion persists during prolonged fasting.

CARLSON (20), has suggested that secretagogues are produced in auto digestion of gastric juice/

juice itself, as well as by the digestive and bacterial processes in the intestine.

PAVLOV (24), demonstrated conclusively that a nervous mechanism was necessary for the production of pyschic secretion, the vagal supply to the stomach being involved alone.

With regard to local, gastric and intestinal stimulation, there seem to be three possible mechanisms.

(1) Nervous Mechanism.

It has been shown by HEIDENHAIN (33), and others that stimuli are still effective in the production of gastric secretion when applied locally to the stomach in the absence of all sympathetic and vagal nerve supply to the part.

Using stomach pouches in which all nerve connections, including the enteric reflexes, had been severed. LIM, IVY & Mc CARTHY (34), showed secretory response to effective stimuli, but the response under these conditions, was less than they would have expected to obtain normally; so that a nervous mechanism does not appear to play an essential part in the mechanism of secretion, though it would appear to be a factor under normal conditions.

(2) Hormone Theory.

EDKINS/

EDKINS (35), and others have found that pyloric extracts stimulate pyloric secretion on injection. The theory postulated as a result of this is that substances, either in the native foods or developed in the gastric digestion of foods, act on the pyloric mucosa in such a way that a gastric secretagogue is produced, and this in turn is absorbed into the blood stream and acts on the glands of the body of the stomach via the blood.

Reviewing the subject CARLSON (20), states that, though the theory may be correct yet all the experimental evidence on which it is based appears to have been completely disproved.

LIM (36), IVY & Mc CARTHY (37), investigating the possibility of a hormone mechanism very fully and using blood transfusion from fed to unfed cats, were unable to find any evidence to support it, but more recently IVY & FARNELL (38), have found that a transplanted stomach pouch would respond to meals by secretion, thus producing strong evidence in support of a hormone mechanism.

(3) Blood Flow.

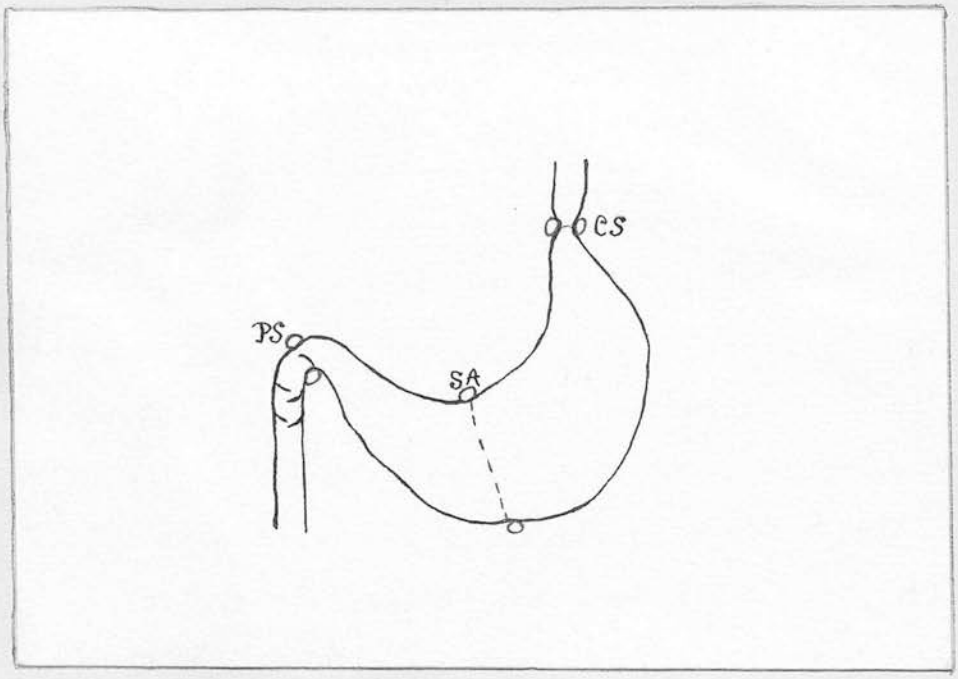
Finding neither a nervous mechanism nor a hormone mechanism entirely suffices to explain the/

the mechanism of secretion, physiologists have made attempts to correlate the vascular changes in the stomach with secretion.

Any evidence in support of this theory is, however, incomplete and inconclusive. Certain isolated observations have been made which suggest a mechanism involving purely circulatory changes. For instance WEITZ & FISCHER (27), have shown that a cold bath increases both the quantity and acidity of gastric juice, and that a hot moist atmosphere lends to inhibit gastric secretion is an observation made by LIM, IVY & Mc CARTHY (39),

Further BURTON OPITZ (40), has shown that gastric distension momentarily increases the blood flow from the gastric veins, and has made the observation that chemicals in the intestine may increase the blood flow in the gastric area. Though the evidence is no more than suggestive, LIM, IVY & Mc CARTHY (37), are sufficiently impressed by such a possibility, to find that although an increased blood flow causing secretion would not necessarily imply increased motility, yet motility may not improbably be invariably related to an increased secretion, either through blood changes or through an enteric reflex.

FIG. 2.



Showing the situation of thickened bands of circular fibres, which according to BURTON & PITZ, develop a sphincter-like action.

CS = Cardiac Sphincter.

PS.= Phloric Sphincter.

SA = Sphincter of Pyloric Antrum.

II. GASTRIC MOTILITY.

THE ANATOMY of the STOMACH.

The musculature of the stomach requires no more than a brief description.

The walls, which consist of three layers of unstriped muscle, are thinnest in the fundus and body of the stomach and become thicker in the pyloric portion. The outer layer of muscle is composed of fibres which run in a longitudinal direction.

The middle layer is composed of fibres which are arranged in a circular manner around the stomach. This layer becomes thickened at the oesophageal and pyloric poles, and in addition there is another thickened band of these fibres situated between the pylorus and oesophagus, at about 7 - 10 cm. distance from the pylorus BURTON OPITZ (41), (FIG. 2)

The inner layer of muscle is composed of obliquely placed fibres which loop over the fundus of the stomach and pass obliquely downwards and to the right. JEFFERSON (42), has noted that the upper part of these oblique fibres are not attached to the other muscular coats, an observation which suggests that functionally they may be separable from the longitudinal/

longitudinal and circular fibres.

THE MOVEMENTS of the STOMACH.

It has been demonstrated by CARLSON (43), that in health, when the stomach is empty, there is continual rhythmical tonus contraction of the body of the stomach. This contraction is very uniform in rate, but variable in amplitude.

In addition he has shown that there are periods of more powerful rhythmical contractions and that these more powerful contractions are identical with the "hunger" contractions of CANNON & WASHBAINE (44),-

It appears that this tonus rhythm is present, not only as a precursor of "hunger" periods, but also throughout the course of normal digestion.

The "hunger" contractions are strong peristaltic waves, starting near the cardiac sphincter and sweeping down over the entire stomach.

He concludes that there is no essential difference between these "hunger" contractions, and peristalsis occurring in the course of digestion (for it has been shown by KASTLE RIEDER & ROSENTHAL (45), that the fundus is not merely exerting a tonic pressure during/

during digestion, and by COLE (46), that contractions begin in the fundus when food is in contact with the cardiac end of the stomach), but that "hunger" contractions are more marked towards the fundus, whereas digestive contractions are mainly concerned with the pyloric region.

This is the view which is now becoming most generally favoured in contradistinction to the older view according to which the muscular wall of the body of the stomach contracts in a tonic manner during digestion, merely exerting a constant steady pressure upon the contents, rhythmic contraction rings only forming in the pyloric antrum.

Recently McCREA, SWINEY, MORRISON and STOPFORD (47), have re-investigated gastric motility, and have reviewed the findings of earlier observers.

They describe two types of motility, a one phase type which corresponds to CARLSON'S view, in that during digestion a wave of contraction starts near the cardiac sphincter and involves the whole stomach, and a two phase type which they describe as follows:-

Deep ring-shaped constructions start from a point just distal to the oesophageal orifice and pass down to the region of the incisura angularis: a deep ring is formed there and remains present throughout/

out the remainder of digestion. The pyloric antrum meantime is seen to bulge out slightly and then this bulging disappears by concentric contractions. Their observations have shown the presence of several waves of ring constrictions in the body of the stomach, while the antrum was in diastole.

Their observations were made on cats, dogs and men, and they found the one phase type of activity constantly present in cats, while apparently both types may be found in dogs and men, though the two phase type of movement is far more frequently present than the one phase type.

It is interesting to record the views of a radiologist in this connection.

BARCLAY (48), states that he is unable to find any functional or mechanical division of the stomach radiologically, though the impression he has received from the general appearance of the stomach, inclines him to support SHERRINGTON'S (49), view of a cardiac reservoir and a pyloric mill.

He finds the function of tonicity and peristalsis, though both produced by functioning of the same muscle, entirely independent of one another, tonicity being distributed over the whole organ, while/

while peristalsis is mainly pyloric in location.

Following JEFFERSON'S (42), observation of the anatomical independency of the oblique fibres, he considers these fibres as not essentially connected with the other coats in relation to tonic action and peristalsis, but as forming a separate sling function for the organ, these fibres forming the essential lesion of the stomach in gastroptosis, as contrasted with general atony of the stomach with which the other muscular coats are more concerned.

THE PYLORIC SPHINCTER.

At present it is generally accepted that, in the presence of food in the stomach the pyloric sphincter will be closed when:-

(a) there are solid masses present in the stomach.

(b) there is insufficient acidification of gastric contents.

(c) when there is acid chyme in the duodenum.

According to the view which CANNON (50) introduced in 1907, the sphincter is controlled by the reaction of the juices on its two sides, and that acid/

acid in the pyloric antrum opens the sphincter, while the presence of acid in the duodenum closes the sphincter. This is the view which is still taught almost universally.

More recently information has accumulated which suggests that the processes of liquefaction and acidification which take place in the stomach, are not the only factors needed for opening the pylorus.

Both in pathological conditions e.g. the rapid evacuation of the stomach in certain cases presenting extremely low acidity, and in the presence of certain matter e.g. water, egg white and fats, results are found which appear to be anomalous to CANNON'S view.

He explains these anomalies on the assumption that conditions not favouring gastric secretion are attended by low pyloric tone.

Several observers have found reason to doubt this acid control of the pylorus, but they have been unable to advance any satisfactory theory as a substitute.

Thus SPENCER, MEYER, REHFUSS & HAWK (51), have found the pylorus opening in the presence of strongly alkaline stomach contents. HANEBORG (52), experimenting/

experimenting in healthy man finds reason to doubt the importance of acid as a factor in controlling the sphincter.

ORTNER (53), finds definitely that the opening of the pylorus is not dependent on the presence of Free HCl in the antrum, and thinks it may be due to the presence of an optimum dilution of gastric contents.

With regard to closure of the pylorus by acid on its duodenal side Mc BAIRD, CAMPBELL & HORNE (54), have noted that acid in the duodenum does not invariably close the sphincter in man.

Mc CLURE, REYNOLDS & SCHWARTZ (55), while testing the effect of various foods upon the opening of the pylorus, find no alteration in their results after placing acid into duodenum and repeating their experiments.

Now LUCKHARDT, PHILIPS & CARLSON (56), have shown in man, that the pyloric sphincter opens for the ejection of chyme with the arrival at the sphincter of powerful advancing rings of contraction and a general increase of muscular tone of the stomach as a whole; and they find that a more definite relation exists between muscular activity and the opening of/

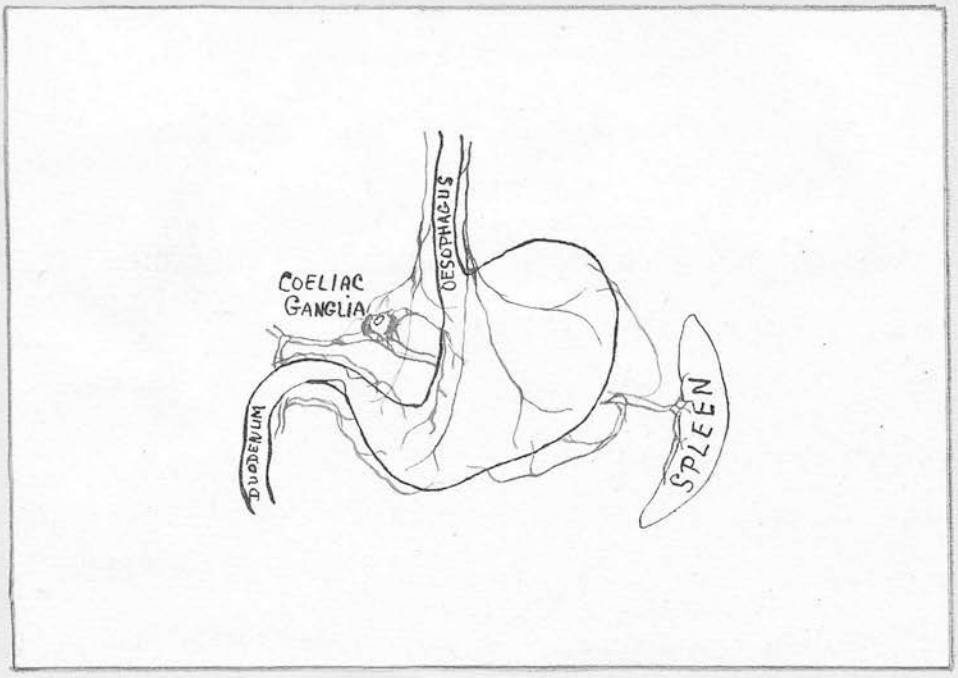
of the pylorus, than between it and the reaction of the gastric contents.

WHEELER & THOMSON (57), finding it generally agreed that, when the sphincter opens, it is peristaltic contractions which discharge the stomach contents through the sphincter, have thought there must be some definite relationship between the activities of the sphincter and intra-gastric pressure, and gastric peristalsis. In dogs they have shown a rhythmical activity of the sphincter occurring in cycles of contraction, relaxation and quiescence, followed by inhibition prior to the next contraction. They find that the sphincter shows tone changes, such changes being gained or lost because of shortening or lengthening of the relaxation phase in the rhythmic cycles.

A mechanism with such rhythmical contractions and tone changes, such as they describe, would account for the intermittent ejection of stomach contents which can be seen so clearly by Xray.

III/

FIG. 3.



Schematic diagram of stomach, showing the general distribution of its extrinsic nerves.

Green = Vagus:

Red = Sympathetic.

The coeliac ganglia are also depicted in Red.

[LIM].

III. NERVOUS MECHANISM.

THE NERVE SUPPLY to the STOMACH.

The stomach is supplied by branches of the splanchnic and vagi nerves.

The right vagus is distributed to the posterior surface of the stomach and BRANDT (58), draws attention to three important branches of this nerve:-

(1) a branch which communicates with the coeliac plexus, and the presence of this possible vagal influence on the ganglion necessitates coeliac-ectomy in certain experimental work.

(2) a branch to the cardiac orifice which he finds may possibly act as an inhibitor to the cardiac sphincter.

(3) a branch which supplies especially the pyloric antrum and canal, and he suggests that this branch may be capable of being thrown into action separately. (FIG. 3)

The left vagus is applied to the anterior surface and lesser curvature of the stomach, along which it is distributed.

These/

These nerves communicate with two anastomosing nerve plexuses. AUERBACH'S plexus which lies intra-muscularly, and MEISSNER'S plexus, which lies in the deeper part of the submucosa. The neurons of MEISSNER'S plexus are very fine and small and are distributed to the mucosa where they terminate about the walls of the blood and lymph vessels and end upon the epithelium of the secreting glands.

JORDAN & FERGUSON (59), KUNTZ (60), suggested that the ganglia of the intra-muscular and submucous plexuses include both motor and sensory neurons, and that those fibres which terminate on the cells of the digestive glands are the dendrons of sensory cells.

More recently KUNTZ (61), has shown the existence of synapses between the ganglia cells in both plexuses, thus leaving no doubt regarding the existence of an enteric reflex arc.

THE NERVE FACTOR in GASTRIC PHYSIOLOGY.

A great deal of the literature upon this subject is inconclusive and in many cases even contradictory.

It has been shown that the central nervous system/

system is not an essential factor for the accomplishment of either gastric secretion or gastric motility.

With regard to the psychic stimulation of gastric juice PAVLOV (22), has shown clearly that the vagi nerves alone are involved.

LIM, IVY & McCARTHY (29), find that, though they are not an essential factor, yet the extrinsic gastric nerves probably exert some controlling influence over that part of gastric secretion at least which is mechanically produced.

Reviewing the literature on the effect of stimulation of the vagi nerves, McCREA, SWINEY & STOPFORD (62), find it generally recognised that stimulation of the vagus results in a motor response of the gastric musculature; some observers recording a preliminary inhibition of movement.

The general conclusion drawn is that the vagi carry both motor and inhibitory fibres to all parts of the stomach, and that no marked vaso-motor changes are involved in stimulation of the vagi.

The writers themselves have conducted elaborate experiments on this subject, and they find that the final effect produced by stimulation of the vagi, is an augmentation or initiation of movement, but/

but that a preliminary effect is first seen, and this may consist of either an augmentation or inhibition of movement, depending on the state of gastric tonus existing at the moment of stimulation.

It does not seem yet to have been shown conclusively that the vagi and splanchnic nerves are antagonistic to one another, and though the splanchnic nerves are commonly thought to be inhibitory to gastric motility, it has yet to be shown (as BURTON OPITZ (41), points out) that such inhibition is not merely apparent and really due to diminished blood supply to the organ, for the splanchnics definitely contain powerful vaso constrictors.

There seems to be little doubt that whatever the factors which control the pyloric sphincter may be, they effect their purpose ultimately by a local reflex through AUERBACH'S plexus.

REVIEW/

REVIEW.

The incursion into the field of physiology, which I have made in securing material for this aspect of my subject, has proved discouraging.

I have been left with the impression that gastric secretion (which forms the main, but not the only consideration of the Fractional Test Meal) has in itself been overstudied, and its value and importance over estimated, to the detriment of gastric tonus.

In this connection it is of interest to note that LIM, IVY & McCARTHY (29), while working upon the question of the mechanical production of gastric secretion, were struck by the fact that when distension was employed for this purpose the same stimulus, namely a condition of tension of the gastric walls, gave rise to both gastric motility and gastric secretion. This observation together with the fact that cold increases both motility and secretion, and that during hunger contractions a larger flow of juice occurs than in quiescent intervals, led them to make the following suggestion. That motility may not improbably be invariably related to an increased secretion, either through blood changes or an enteric reflex, although an increased blood-flow causing secretion/

secretion would not necessarily imply increased motility.

Further RYLE [63], has compared the results of the investigation by MOODY, VAN NUYS & CHAMBERLAIN [64], into gastric tonus in healthy males, with those of BENNETT & RYLE [65], upon the secretory curves in a similar normal series.

With regard to tonus the findings were - orthotonus 79%; hypertonus 17%; and hypotonus 4%. while with regard to acidity in the other series of cases - normal acidity 80%; hyperchlorhydria in 15%; and hypoacidity or achlorhydria 5%. These figures are strikingly suggestive of a close relationship, and CAMPBELL & CONYBEARE [66], have been able to establish some definite correlation between tonus and acidity in yet another series of cases.

That greater importance should be attached to gastric tonus is at least hinted at by several observers and there seems to be a large gap in our knowledge where tonus is concerned.

The question of tonus itself probably requires a more complete understanding of the nerve factor in relation to the stomach; a factor concerning which I have been able to find little that is definitely/

definitely established.

The bearing that physiology has upon points to be considered later in this paper will be mentioned as occasion arises.

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THE PHYSIOLOGY of the STOMACH.

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THE FRACTIONAL METHOD of GASTRIC ANALYSIS.

VARIOUS GASTRIC SECRETORY and GASTRIC MOTILITY TESTS.

In considering this subject some of the earlier methods of securing gastric secretion in normal man form an interesting historical back ground.

As early as 1780 SPALLANZANI (1), was able to demonstrate that gastric juice was acid, that it digested food, that it was a preventative of putrefaction, and that gastric digestion depended in part at least upon chemical changes.

To obtain gastric juice he employed a variety of methods; vomiting was produced and the vomited matters used in some cases. In others sponges or food in perforated wooden or metallic capsules were swallowed and these were recovered for examination of the changes, either by having threads attached to them, which allowed them to be pulled up, or forced up by vomiting, or being passed per rectum.

Such methods as these obviously lacked any degree/

degree of precision or refinement, and were not calculated to advance the study of gastric conditions clinically. In fact little advance was made clinically till von LEUBE [2], employed a tube for securing gastric contents, though in the meantime BEAUMONT'S observations on his fistula case and experimental work in animals by other observers had advanced the subject along physiological lines.

The actual introduction of a tube into the stomach appears to be a feature of considerable antiquity, but prior to von LEUBE'S work the tube was used exclusively for feeding and for gastric lavage, but he employed the tube for removing gastric contents for analytical purposes.

Following LEUBE'S technique EWALD [3], BOAS and the German gastro enterologists devised means of establishing the use of the tube in a more standard test, thus enhancing the value of the results obtained. They conceived the idea of using a constant stimulus and examining the response at a definite interval. For this purpose they used a standard "test breakfast" and withdrew the stomach contents an hour later, at which time the maximum secretory response was usually obtained. This form of/

of gastric secretory test is the one which is in common use at the present time

Various slight modifications have been made by different observers, but the principle remains unchanged. Thus the outside diameter of the tubes now in use varies from ¼ to ½ an inch, some clinicians finding a relatively larger tube easier to insert, less uncomfortable to the patient, and ensuring greater success in removing the stomach contents. Variations, too, are common both in form and number of openings at the gastric end of the tube.

The form of the "test breakfast" itself has been the subject of many changes, though EWALD'S test meal - "a roll or piece of bread or toast (about 35 gms.) without butter, and two cups of water or tea (about 300cc.) without milk or sugar" - is still, perhaps, most frequently employed.

BOAS test meal of oatmeal does away with the possibility of lactic acid formation from bread.

RIEGEL'S test meal was introduced with a view to giving the patient a closer approximation to his normal diet. While FISCHER'S meal arranged for the same purpose, is said to give more constant results (FAUGHT)[4].

BERGHEIM/

BERGHEIM, REHFUSS & HAWK [5], have tried the substitution for the meal, of water alone thus attempting to overcome the undesirable admixture of test substance with gastric juice, but their results were subject to the disadvantage of not showing the effect of food stimulation in the production of gastric response.

Further other observers IVY, MOFFAT, MITCHELL & POWELL [25] [26], find the results of water stimulation are too variable for it to be employed as a test. So though this form of test has been in use now for many years, it will be seen from the comparative unimportance in the modifications which have been made in it, that there is little hope of any marked advance in our knowledge of gastro enterology being obtained through its continued use.

It is interesting to note that these earlier observers were impressed with a desire to be able to follow through the "digestive cycle" more completely. LEUBE himself apparently attempted a form of fractional analysis, removing portions of the test meal at fixed intervals, but the dimensions of the tube make it too uncomfortable to retain in place for any length of time, and the difficulty in swallowing/

swallowing such a tube prohibits its passage at frequent intervals. EWALD, too, attempted a form of fractional analysis by repeating the same meal on succeeding days, and removing the contents of the stomach at different intervals, but this clearly was not practicable on more than an experimental scale, though more recently a similar procedure was adopted by HAYEM (6), and he was able to publish fairly extensive reports of his findings.

With the advent of a small bore and flexible tube, however, fractional analysis of stomach contents was placed on a practical basis.

It appears that as early as 1893 GROSS (7), had reported on the use of a soft nelaton catheter for this purpose. It was not until 1914, when REHFUSS (8), recorded his modification of EINHORN'S duodenal tube, to the purpose of gastric analysis, that this fractional method attracted any attention in this country or America, though at a slightly earlier date EHRENREICH (9), had aroused interest in this method in Germany.

In consulting REHFUSS' original paper I was interested to find that he himself apparently was not entirely convinced of the success which would follow/

follow his suggestion, for fully two thirds of his paper deals with a modification of a perforated metallic food-containing capsule to be removed from the stomach by thread. Impressed with the need for some method of examining gastric contents, which would obviate the use of the large stomach tube, he was endeavouring to improve on the existing methods of examination. The large stomach tube he describes as too irksome to the patient, and as apt to cause temporary upset in some persons, for cases requiring a minimum of disturbance or inconvenience it was quite unsuited, and some observers had produced an overwhelming number of contra-indications to its use.

The other existing methods of gastric secretory examination were all on the principle of either SPALLANZANI'S sponges, EINHORN'S buckets or DURHAM'S indicator threads. These, to his mind, were all subject to the big disadvantage of being contaminated by pharyngeal mucus, and the feature of his metallic capsule upon which he lays most stress is, that the contents of the capsule are free from contamination from this source, but that section which has proved to be the important part of his paper receives relatively scanty mention.

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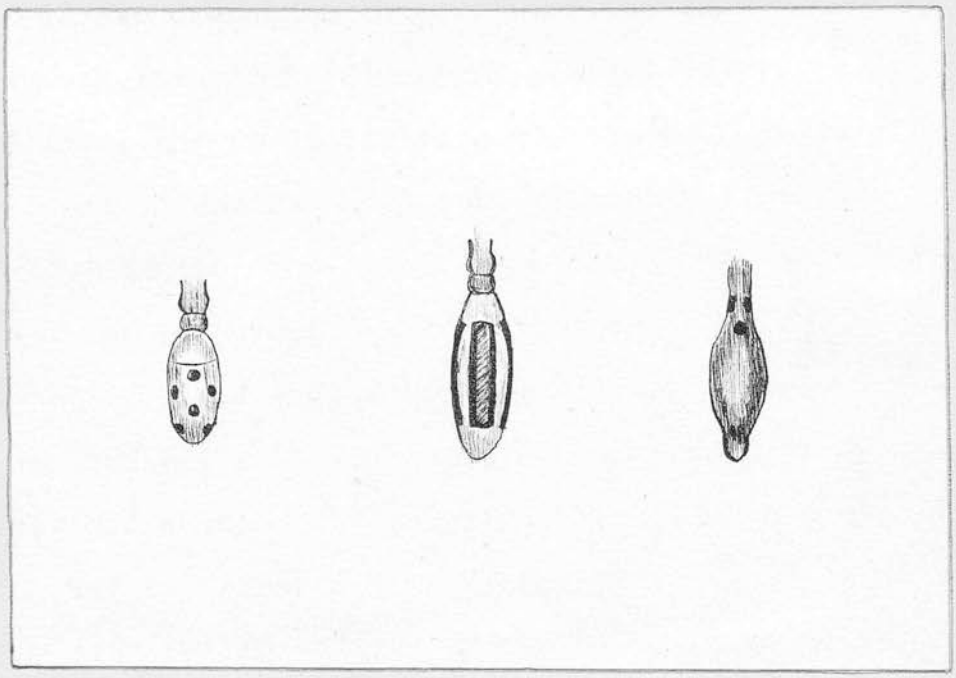
FIG. 4.



Various modifications of the tube tip employed in conjunction with the narrow bore gastric tube. (sketched full size.)

LEFT: EINHORN'S Metallic Tip with small round perforations.

CENTRE: REHFUSS' modified metallic tip with slotted perforations.

RIGHT: RYLE'S modification, rubber-covered with small round outlets in the rubber itself.

The modifications of EINHORN'S duodenal tube, which he devises to permit of its use for gastric work, consisted in alterations to the metallic tip of the instrument. The perforations in the tip of the existing instrument were large enough to allow the withdrawal of duodenal contents, but they were so small that it was impossible to aspirate more than scanty frothy specimens from the stomach. To overcome this difficulty REHFUSS used a tip with slotted perforations in it, the diameter of the slots being as great as the caliber of the tube (FIG. 4). In addition he added to the weight of the metallic end, for he found this made it easier to swallow and also ensured that gravity would make it lie in the lowest level of the stomach.

Within a short time, using this modified tube in conjunction with BERGHEIM & HAWK, he developed the technique of fractional analysis, and the fractional test meal method of gastric examination was placed on a practical basis.

This was not the only valuable advance made by the new tube, for HARMER & DODDS (10), had shown that the old thick tube was apt to curl up in the/

the stomach, and so give fallacious results in attempts to evacuate completely stomach contents, whereas REHFUSS, BERGHEIM & HAWK (11), now showed that the principle of the tube was entirely that of gravity, and that the tip of the tube was sufficiently heavy to make it exert its suction from the lowest part of the stomach.

More recently RYLE (12), has still further modified this small tube, he uses a narrow bore No. 8 French, rubber tube with a blind-end, into this blind expanded end an oval lead weight is inserted, and at a distance of about 2cm. from the tip it is perforated by several holes of about 2mm. diameter. (FIG. 4).

The advantages claimed for this tube are that it is more easily swallowed and withdrawn, that the openings being in elastic walls there is less likelihood of them becoming blocked, and that if blockage does occur it is easily overcome by air pressure; that the end cannot become detached, and that there is no likelihood of strong suction in an empty stomach producing trauma of the mucous membrane.

The form of stimulation to be used in conjunction with fractional analysis has not been modified to any extent, and EWALD'S or BOAS "test breakfasts" are still most commonly used for this purpose, but/

but a slightly modified form of BOAS'meal, which will be described in detail later, would seem to give the best results.

At this stage it may be well to consider the effect of fractional analysis in relation to the study of gastric motility.

Apart from radiological methods of estimating gastric motility, several tests have been advised for this purpose. The "one hour" test meal as usually conducted will give evidence of gross changes in motility, and its value from this point of view may easily be enhanced by giving the patient some readily recognised substance in their dietary at some period of hours prior to the test. Further substances such as salol and iodoform may be given by mouth and the time recorded till the appearance of salicylic acid in the urine, and iodide in the saliva respectively.

The advantage of fractional analysis , as a test of gastric motility alone, over these methods is clear, and while it may hold no definite advantage over Xray methods in this sphere, yet there is ready scope for a test which provides for the study of gastric motility, and gastric secretion at the same time/

time.

In this connection it is interesting to record the results of motility tests performed in a large series of patients seen at the Mayo Clinic in 1914. The motility was tested both by Xray examination after bismuth given six hours previously, and by the passage of a large stomach tube about twelve hours after the ingestion of easily recognised food. e.g. raisins (this being the form of motility test in general use at that time, apart from Xray examination). In this series of cases it was found that Xray examination recorded 70% more retentions than were shown by the test meal, demonstrating the gross inaccuracies to which the stomach tube test was liable CARMAN (13).

RUSSELL (14), on the other hand, finds that a bismuth meal is got rid of by the stomach in a much shorter time than an ordinary meal of mixed foods, so on the understanding that the REHFUSS or RYLE tube is capable of evacuating completely stomach contents, it would appear that fractional analysis may be at the present time the most accurate test of normal gastric motility.

Now, however, satisfactory fractional analysis/

analysis, as outlined above, may prove as a practical test of gastric secretion, it is open, nevertheless, to severe criticism as a test for this purpose, when judged from a purely physiological standpoint. The various loopholes for inaccuracies in this test, will be discussed in some detail later, but I will draw attention here to two points which place the test, scientifically speaking, upon an unsound basis; namely that the fractional samples examined for gastric secretion are contaminated by food, and may be contaminated by regurgitated duodenal juices.

Recently investigations have been made with a view to eliminating these possible sources of error.

Several observers EINHORN (15), CARNOT, KOSKOWSKI & LIBERT (16), have endeavoured to overcome the difficulty of duodenal regurgitation by using two tubes, one lying in the duodenum and the other in the stomach, but since the duodenum was only emptied intermittently in this case clearly regurgitation was still liable to occur.

LIM, MATHESON & SCHLAPP (17), however, have devised a technique in which, with one tube in the stomach and one in the duodenum, continuous suction is/

is applied to both tubes, so that the contents of the duodenum are removed as soon as they appear, without ever coming imto contact with the contents of the stomach.

With regard to elimination of food contamination, MATHESON & AMMON (18), have shown that histamine acid phosphate injected subcutaneously in man, produces marked gastric secretion accompanied by an increase in HCl and peptic activity. Further LIM, MATHESON & SCHLAPP (17), find that histamine, used in this way in man, produces a pure gastric secretion which resembles "appetite" juice in all respects.

So that the most accurate method, at present available for testing gastric secretion in normal man, would appear to be intubation of both stomach and duodenum with continuous suction applied to both tubes, together with the subcutaneous injection of histamine as a stimulant to secretion.

There are, however, at the present time, certain objections to this most accurate test being employed upon more than an experimental scale. It is not uncommomly difficult to persuade a patient to swallow/

swallow a single tube and the alarm occasioned by the presence of a second tube, and the apparatus for producing continuous suction would be insurmountable in some cases. While it is not possible in all surroundings to fit up a suction pump, requiring as it does, a constant water supply. Further, the effect of histamine in pathological conditions has not been fully investigated as yet. It has been noted that suitable doses of histamine show no harmful effects. (LIM, MATHESON & SCHLAPP [17]; MATHESON & AMMON [18],) though BENNETT & DODDS [19], find that the injection is followed by immediate intense flushing of the face, and a quickening of the pulse. LIM, MATHESON & SCHLAPP [20], investigated the effects of the drug in nine cases of suspected carcinoma, but apart from these observations little is recorded about the effects of histamine clinically.

So that for practical purposes the passage of a single tube into the stomach, with a "test breakfast" as a stimulus and the withdrawal of gastric contents intermittently, remains the most satisfactory gastric secretory test, and in addition this test may afford valuable information regarding gastric motility.

For/

For the sake of completeness it is advisable to mention two other forms of gastric test.

One test which has been introduced recently by DODDS (21), depends upon an entirely different principle from any of the methods already outlined by me.

By taking samples of alveolar air, at intervals after a meal, DODDS was able to show that the tension of Carbon Dioxide in the alveolar air undergoes certain definite changes in response to the amount of secretion poured out by:-

(a) the stomach.

(b) the lower portion of the alimentary tract.

One of the chief advantages of this test is that it can be used with a minimum of discomfort or inconvenience to the patient.

In pathological conditions he finds results by this method are at least as characteristic as these obtained by means of a fractional test meal, but this test has not met with general favour as yet, and it is impossible to estimate its relative value at present.

The other test may be placed in the same category from the point of view of practical application/

application. It depends in principle upon the estimation of the acidity of gastric contents by means of the H-ion concentration determined by the gas-chain method. McLENDON (22), devised an electrode which could be introduced directly into the stomach, and in this way determined the H-ion concentration of the gastric contents in situ. Apart from certain observations made by McLENDON himself this method does not seem to have been used further.

The TECHNIQUE ADOPTED in this SERIES of CASES.

The general procedure carried out may be briefly summarised thus.

A RYLE pattern of tube was passed into the stomach and all the contents of the resting stomach were withdrawn.

The stomach was stimulated to secrete by means of a modified BOAS' meal. Samples of gastric contents were then withdrawn at intervals of quarter of an hour, and various tests were applied to the material obtained in this way.

The practical procedure adopted will now be considered in greater detail, under the following headings:-/

headings:-

(1) The preparations made for the test.

(2) The passage of the tube, and the withdrawal of samples.

(3) The method of examining the stomach contents.

(4) The Repetition Test Meal.

I. The PREPARATIONS made for the TEST.

In order to allow adequate preparation to be made before hand, the test was almost always ordered for "the day after tomorrow".

In the evening upon which the order had been given, the patient received any drugs he might be having, and if necessary he might get a mild laxative - but no strong purgative. On the following day he received no drugs whatsoever, and his diet was a simple light diet - usually containing no meat, red or white, because his stools were being tested for occult blood during this period.

On the day prior to the test it was my custom to explain the nature and purpose of the test to the patient. The majority viewed the prospect with complete equanimity, some offering to swallow anything/

anything that would help towards their cure, while others were quite evidently perturbed at the thought of the procedure required.

With a view to alleviating this alarm, which the suggestion aroused in some patients, I endeavoured to arrange that each patient should see some other patient in their ward emerge unscathed from the ordeal. Also I encouraged nervous patients to discuss "the tube" with their neighbours, and I found frequently that this served to set their minds at rest.

At 11 p.m. on the night before the test the patient was given a cup of milk containing two teaspoonfuls of charcoal, and a charcoal biscuit, though the eating of the charcoal biscuit was not insisted upon.

I followed BENNETTS' (19), custom of asking all patients not to brush their teeth in the morning, prior to the test, lest blood be introduced to the stomach from this source.

II./

II. THE PASSAGE of the TUBE and the WITHDRAWAL of SAMPLES.

The test was commenced at 6.30 a.m. which was the hour most suitable for the routine of this hospital.

The patient sat upright in bed, and was asked to place the bulbous end of the tube, together with two or three inches of the tubing, in his mouth, and leave it there for a few moments, to get thoroughly moistened by saliva.

The tube I used was a No 8 French rubber tube, the bulbous end being that devised by RYLE, which I have described already. It is marked by a transverse line at 40cm. and 57cm. distance from the tip to indicate approximately the cardiac orifice and the pylorus respectively. The tube was boiled and kept lying in warm water till given to the patient.

The patient was then asked to work the bulbous end in his mouth towards the back of his tongue, and to keep two or three inches of tubing slack in his mouth by pursing his lips firmly round the tubing. The suggestion was then made that he swallow the bulb as he would a pill, and should he succeed/

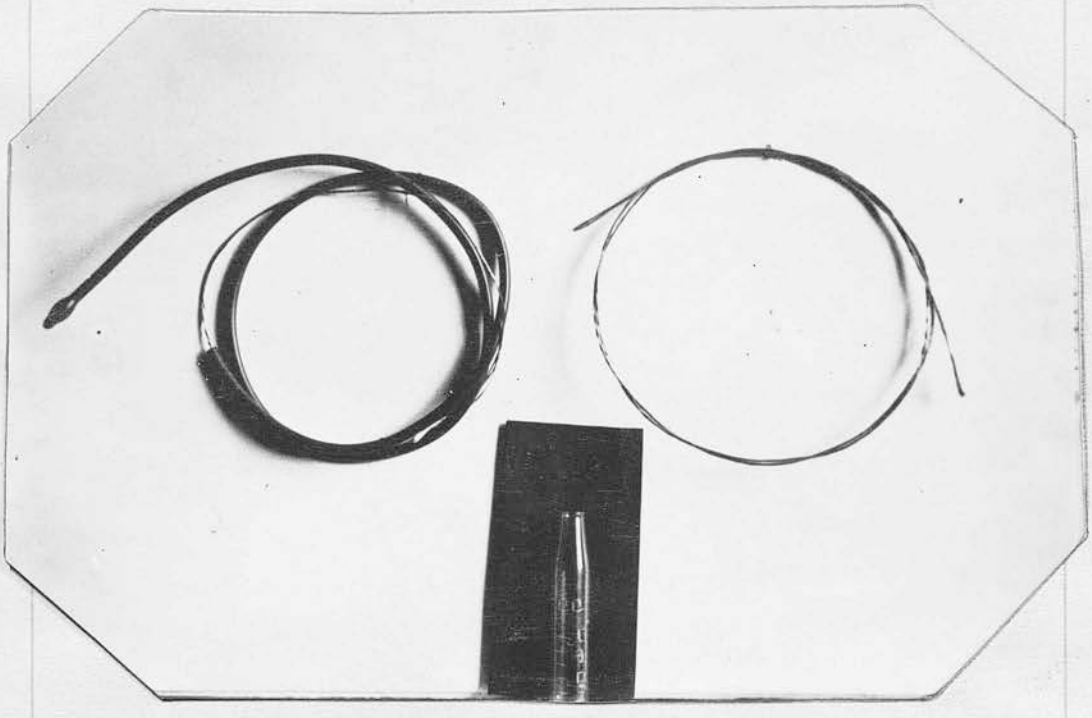
succeed in "getting it over" he was to swallow several times in quick succession,(with a view to getting the bulb rapidly past the construction corresponding to the cricord, at which point sticking is most likely to occur) RYLE (23) .) and then pause and take long breaths to assure himself he could breathe freely. Having paused for a few moments he was to continue to swallow without undue haste, till the mark indicating the pylorus was just at his lips; if he felt any inclination to retch he was to stop swallowing and take several long breaths again.

A few patients undergoing the test for the first time, succeeded in swallowing the bulb at the first attempt, in the majority two of three attempts had to be made before they succeeded.

In a few patients, who were unsuccessful after several attempts along these lines the addition of a little glycerine to the end of the tube made all the difference.

Repeated abortive abortive attempts to swallow the tube are to be deprecated, however, even though success may be achieved in the end, for the patient becomes greatly upset, and coughs and retches in a distressing manner, calculated to produce"emotional/

FIG. 5.



RIGHT: Bowden wire stelette coiled up to show flexibility. The small blob of solder can be seen at each end.

LEFT: A Ryle tube with a stilette in situ. It will be observed that the free weighted end of the tube is not hanging down vertically, but has received a certain amount of rigidity from the stilette inside it.

CENTRE: A Five cubic centimetre flask (from an Ethychloride anaesthesia apparatus) which has proved a convenient measure for gastric contents.

"emotional disturbance" of gastric secretion, and to make a second test meal quite impossible.

To obviate this disturbance I devised a form of stilette which allows the tube to be passed down the oesophagus for a few inches, after the manner of the old large size stomach tube,

This stilette is made of six strands of fine Bowden wire twisted together and cut to a length of about three feet. The sharp ends of the strands are crushed together, and covered and held in place by a small blob of solder. (FIG. 5)

The stilette is passed down the tube until the soldered end comes to rest up against the lead weight at the end of the tube, and has passed beyond the small apertures at the gastric end of the tube.

It will now be found that though the rigidity of the tube has been increased by the introduction of the wire, yet it has lost little of its flexibility. It appears that DOTT (24), has used a nickle wire for this purpose, but has been disappointed by his results.

When the stilette has been inserted into the tube, the fit may be tested by holding the wire up by the free end, when a gentle shake should make the/

the tube slide off the stilette. If this does not occur the addition of a little glycerine to the end of the wire, prior to its insertion into the tube, should have the desired effect.

With the wire in position the tube is made rigid enough to allow of its being pushed back against the posterior pharyngeal wall, and so into the oesophagus; meanwhile the patient is asked to breathe deeply.

After the tip of the tube has passed about six or eight inches beyond the teeth, the stilette is withdrawn, and the patient proceeds to swallow the remainder of the tube slowly and steadily in the manner already described.

When the tube had been swallowed as far as the pyloric mark, suction was commenced, by means of either a Record or an all-glass syringe. I found an all-glass syringe the more useful, as the Record syringe tended to become blocked and crusted with fine particles of the aspirated meal, and it was more difficult to clean effectively after coarse work of this kind.

In an effort to empty the stomach entirely suction/

suction was applied with the patient sitting up at first, then lying on his back, then on the left side, then on the right side, and finally lying round on his face; no change of position was made until suction in the existing position produced only a little froth. During this preliminary emptying of the stomach the tube might be withdrawn a few inches, or swallowed a few inches past the pyloric mark, in order to search the stomach thoroughly for contents. After this procedure the patient was asked to maintain the tube at the pyloric mark, and to spit out any saliva rather than swallow it.

Of the aspirated resting contents the first 15 - 20c.c. were placed in a test tube, marked "O", and the remainder of the resting contents were placed in a bottle similarly marked.

The patient then sat up, and with the tube still in situ, ate his "test meal". The meal consisted of thin gruel, made by adding two level tablespoonfuls of oatmeal to two pints of water, and allowing this to boil down slowly to a pint in amount, (this will take several hours); this pint of gruel was then strained through muslin. Though no estimation/

estimation of chlorides was being undertaken in the present series of cases, no salt was added to the meal for the sake of uniformity. A meal of this nature is not very palatable, but it possesses the great advantage of giving a colourless filtrate when examined later, and consequently titration end points can be defined more sharply.

After taking the meal the patient was asked to lie down again, and to remain lying for the rest of the test, again for the sake of uniformity, reading or talking being encouraged to minimise psychical disturbance.

The tube itself was clamped by a pair of light artery forceps, to prevent any leakage of gastric contents. The handle of the forceps was then pinned to the collar of the night attire or else held by the patient.

Samples were then withdrawn through the tube, at intervals of quarter of an hour, reckoned from the time at which the patient commenced to take the meal. Care was taken to see that the pyloric mark was at the level of the teeth before each sample was withdrawn, and the syringe was washed out after use each time.

Samples/

Samples were withdrawn in this way for two hours, i.e. eight samples were obtained each consisting of 15 - 20c.c.

The advisability of continuing the withdrawal of samples for a longer period, or until the entire stomach contents had been evacuated in fractions, was considered, but the extra work of preparing proper breakfasts for patients at irregular times made this method undesirable. Further it was thought that by fixing a definite period of two hours for the test, the results obtained would be more uniform, and that the findings would suffice both for the purpose of the present investigation, and from the point of view of diagnosis.

These samples were placed in test tubes numbered "1", "2", "3", and so on , according to the order in which they were obtained.

After sample No "8" had been removed the stomach was emptied as rapidly and as completely as possible; to do this the patient was put through the various positions mentioned when emptying of the stomach prior to the test meal, was being referred to.

The contents obtained in this way were placed in a bottle marked "8". The tube was then withdrawn/

withdrawn with a rapid movement.

III. THE METHOD of EXAMINING the STOMACH CONTENTS.

The samples for examination were contained in nine test tubes, marked "0", "1", "2", and so on to "8", and in two bottles marked "0" and "8" respectively.

It was my custom to proceed as follows:-

The patients name and the date of the test were entered on a sheet of paper, which contained ten columns, one for each of the test tubes, and one for bottle "8".

The naked eye appearances of the specimens were then noted, each was examined for the presence of the various yellow and green shades of bile, for the presence of blood either staining the specimen throughout, or in minute flecks only.

The specimen from the resting stomach was also examined for the presence or absence of charcoal.

The nature of each specimen, whether "clean"/

"clean" or "dirty" was estimated roughly.

Each tube sample was then tested quantitatively for "free HCl" and "total acidity" by titration against decinormal N A O H, using dimethyl-amido-azobenzol. (TOPFER), and phenolphthalein solutions as indicators respectively. Amounts of 5 c.c. of the sample were used on each occasion, and I found the 5 c.c glass phial of an ethyl chloride anaesthesia apparatus very useful as a measure for this amount. (FIG. 5).

Using this phial there was a minimum of unnecessary contact between the sides of the measure and the gastric sample, such as occurs in using a larger or taller measure for this purpose. After the measured contents had been poured into a porcelain basin the phial was filled with 5 c.c. of water, the top closed by a finger, and then shaken thoroughly. This water was then added to the sample in the basin.

The presence or absence of mucus in each sample was judged from the behaviour of the fluid while being measured out, and was noted.

This phial, the porcelain basin and the glass rod, used during the titration were washed through running water after being used for/

for each sample.

The acidity values were recorded in cubic centimetres of decinormal N A O H per 100c.c. of stomach contents.

In any specimen in which the amount of "Free HCl" was found to be very small, or in which the colour changes were obscured by the presence of charcoal and stagnant food, the phloroglucin-vanillin test was performed before the (GUNZBURG) reaction to TOPFER'S reagent was recorded as positive.

The amounts of gastric content in bottle "O" and tube "O" were measured in cubic centimetres, and these amounts added together were recorded as "Resting Content", while bottle "8" and tube "8" were treated similarly and the amount recorded as "Residue".

Finally a few drops of iodine solution were added to each tube, and to bottle "8" to show the presence or absence of starch, with a view to estimating the emptying rate of the stomach.

The particulars obtained by these methods were marked in an abbreviated form upon a chart, and the figures denoting the quantitative amounts of "Free HCl" and "Total Acid", were translated into a graph by being plotted against a time basis on the same/

IV. THE REPETITION TEST MEAL.

The most noteworthy feature of the present series of cases, was that a second test was performed, the technique of which was similar in all details to that which I have just described.

This repetition test meal was given on the morning following the first test when possible.

As the nursing staff were unable to cope with more than two test meals on any one morning, not infrequently two or even three days had to elapse between tests in any one case.

The greatest possible care was taken, however, to obtain a maximum uniformity of technique, and of circumstances attendant upon the two tests in each individual.

THE FRACTIONAL METHOD of GASTRIC ANALYSIS.

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THE FEATURES of the FRACTIONAL ANALYSIS CHART.

When the results obtained from the test have been transfered to paper and summarised graphically, the next step to be taken is their interpretation clinically.

In this thesis I am not so much concerned with the mode of interpretation, as with an analysis of the features of the chart upon which this interpretation depends.

Because it is the constancy of the features in each particular case which is being investigated more particularly.

Briefly the points to be noted on the chart are, the acidity curves, the persistence of starch in the samples, the presence of charcoal, blood, bile etc., at any time during the test; the amount of the resting content, and the residue at the end of two hours; and the general appearance of the samples.

When these features are traced from their genesis up till the time they are recorded on the chart, they are seen to be exposed to various fallacies.

Each/

Each feature of the chart will now be considered in greater detail, and possible fallacies in the various points will be discussed as occasion arises. Whenever possible I shall use charts obtained from the present series of cases to illustrate particular details.

The subject will be dealt with under the following headings:-

I. The Curves of Acidity.
II. Starch.
III. Charcoal.
IV. Bile.
V. Mucus.
VI. Blood.
VII. The Resting Content; the Residue at two Hours, and the General Appearance of the Samples.

I. THE CURVES of ACIDITY.

The acid curves are considered to be indicative of the acid state of the stomach during the digestive phase following a known stimulus.

This/

This acid state is dependent primarily upon two factors, namely, acidity from the gastric secretion, and neutralisation from other sources.

The acid is produced as part of the gastric juice, and it is generally accepted, that pepsin content of gastric juice increases in amount under stimulated conditions, along with the acid content LIM[1], (and the functional dependency of pepsin upon acid secretion adds weight to this conception)

So that, in so far as the curves give any indication of the acid response by the stomach, they may be taken to give an indication of gastric secretion as a whole.

It may be said at once, however, that though the curves may be expected to give a reasonably accurate idea of the acid state of the stomach, (despite possible fallacies which are to be discussed), yet the indication of gastric secretory response which they give may be markedly distorted.

Further, the stimulus employed cannot be counted as an entirely known and constant quantity, and it will be convenient to discuss the stimulus in the first place.

THE/

THE STIMULUS.

With a view to obtaining results which will be of value for comparative purposes, a meal of standard chemical composition and of standard bulk is used, and this is assumed to form the sole stimulus to secretion in each case.

There are, however, other factors outside our control, which may affect the actual resultant degree of stimulation.

(a) Under the heading of Effective Stimuli to Secretion, I made mention of the failure of foreign bodies in the stomach to produce secretion.

This view is supported by PAVLOV (2), as a result of his experiments in animals. CARLSON (3), also finds that these mechanical stimuli may not be adequate for secretory response, but suggests that they are indeed violent enough to produce inhibition, and in view of the fact that PAVLOV (2), did not record observing any normal fasting secretion during his observations, an inhibitory influence seems conceivable.

BEAUMONT (4), in his original observations many/

many years previously records his opinion as being "that the irritation of tubes etc. is local and produces only a partial excitement of the vessels, and a scanty flow of gastric juice".

He did not, however, control the fasting secretion in his work, nor did several observers SCHIFF (5), TIEDEMANN & GMELIN (6), who have recorded secretion due to stimulation by foreign bodies in the stomach.

More recently LIM, IVY & McCARTHY (7), record that wooden heads, of a size sufficient to impede gastric contractions, provoke secretion. While IVY (8) and LIM, MATHESON & SCHLAPP (9), found a slight augmentation of secretion, which lasted for rather less than an hour, following intubation. In their investigations fasting secretion was controlled adequately, but they observe that this secretion following intubation might be due to a reflex consequent on swallowing the tube.

The general consensus of opinion seems to favour the view that intubation itself probably causes no secretion, while it would appear that any/

any secretion it might produce would be insufficient to interfere with practical results.

(b) Psychic secretion has been referred to already, and it may be recalled that CARLSON (3), came to the conclusion that "seeing, smelling and tasting food induces gastric secretion, provided that the state, hunger or appetite is present. Tasting food seems to be the most potent stimulus in most individuals; seeing & smelling food may be without effect in some persons".

Other observers BENNETT (10), VENABLES & RYLE (11) have not been able to demonstrate true appetite secretion in normal man. So that it may be inconsistently produced, or at least only slight in amount.

Further CARLSON (3), found that the latent period, prior to its production was probably less than five minutes, while it ceases usually within fifteen minutes, so that if appetite secretion does occur it will have ceased before the second specimen of the fractional test has been withdrawn.

While the insipid nature of the test meal, and/

and the fact that it requires no chewing suggests that in even in the state of hunger it would produce a minimum of appetite secretion.

(c) The effect of emotions, such as fear and anger upon gastric peristalsis has been demonstrated clearly by CARLSON (3) and CANNON (12), so that the possibility of emotional factors producing alteration in secretion seems not improbable.

BENNETT & VENABLES (10), have attempted to estimate the effect of unpleasant emotions e.g. nausea, anxiety, by using hypnotic suggestion,& they find definite inhibition to secretion produced in these cases, but they were unable to satisfy themselves that pleasant suggestions produced secretion. HEYER (13), obtained similar results in hypnotised persons, but found inhibition of secretion produced by both unpleasant and pleasant suggestions, though the former produced a more marked depression of secretion. LUCKHARDT & JOHNSTON (14), however, find that the suggestion of eating a meal produces in hypnotised persons a copious secretion.

The/

The somewhat contradictory nature of these observations suggests that either the effect of emotional disturbance upon secretion is not great or else it is dependent upon a personal factor.

While the test meal given is not calculated to promote appetite secretion, yet in no case which I have seen has there been any suggestion that the meal itself was so objectionable as to produce definitely unpleasant feelings. So that the very negativeness of the gustatory sensations aroused by this meal may be a factor of some value in making for uniformity of stimulation.

With reference to any emotional stresses, consequent on the circumstances of the test, RYLE (11), finds these not significant. He records that among "many hundreds of cases" there were less than half a dozen in which emotional upset prevented the swallowing and retention of the tube, and that gross variations in the curves, which could reasonably be attributed to mental or physical distress have been rare.

My own observations, during the tests in my present series of cases, are in accordance with those/

those of RYLE (11), There has been one occasion only on which a patient was unable to swallow the tube. This particular patient was a women, at the menopause, whose symptoms included vague abdominal discomfort; in her case there was no nausea or retching when given the tube, but rather a complete disinclination to attempt to swallow it. It was noteworthy that abdominal discomfort ceased to appear in her list of symptoms, and her ultimate diagnosis was hysteria.

In a few of the earlier cases in this series swallowing of the tube was accompanied by slight retching, and I anticipated finding perceptible differences between the first and second test results, which might reasonable be attributed to this cause.

It was for this reason that I devised the stilette which I have described already. On the occasion of their second test, patients either showed no distressing symptoms or else these were present in slight degree only.

In this connection BENNET & RYLE (15), write:-

"Time/

"Time after time we have seen a subject have considerable difficulty in swallowing the tube for the first time, and yet, having once succeeded he has been able to repeat the performance on subsequent occasions without the slightest trouble". (Unfortunately the results obtained from tests on subsequent occasions have not been published by these observers, so far as I can discover).

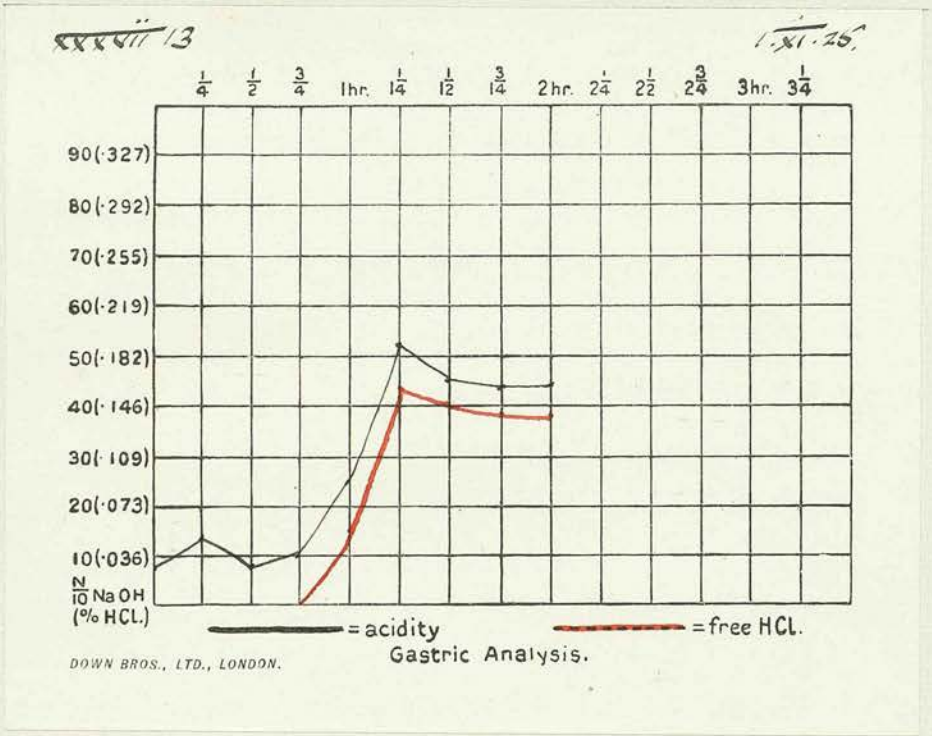
However I was unable to establish any relationship between the results obtained and the degree of distress during consecutive tests in any one case, and such differences as I did find were not invariably in the direction of diminished secretion in the first test.

In this connection I may draw attention to three cases as being noteworthy.

All three patients showed definite distress while swallowing the tube for the first time, while they all experienced relatively little difficulty on the second occasion. In two of these cases the acid curve from the first test suggests definitely/

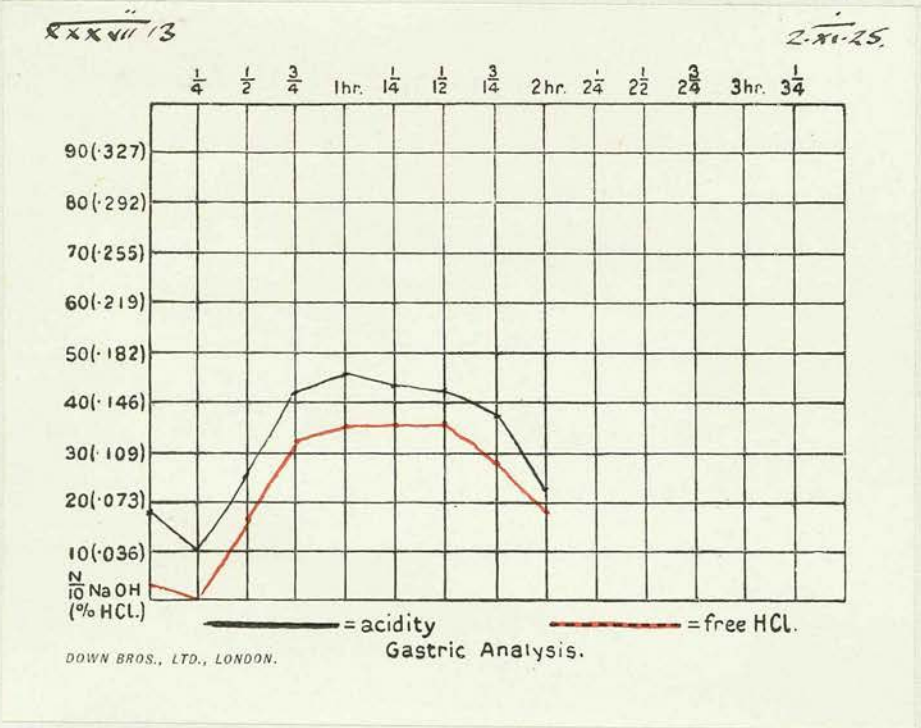
71a

71A
CHART I.



I

CHART II.



II

definitely a temporary inhibition of secretion from some cause, and these are the only two cases in which I have found this type of curve which is characterised by a definitely low acid state during the early part of the test with a relatively high acid state making a delayed appearance.

CHARTS I. & II.

CASE (II).

Male aged eighteen years. Diagnosis of "Habit Dyspepsia".

CHART I obtained on 1.XI.25. When patient had considerable difficulty in swallowing the tube.

CHART II obtained on 2.XI.25. When patient swallowed the tube quite easily.

CHARTS III. & IV.

CASE (XL).

Female, aged thirty eight years. Diagnosis of Acute Gastric Ulcer.

CHART III obtained on 16.X.25. When patient/

CHART III.

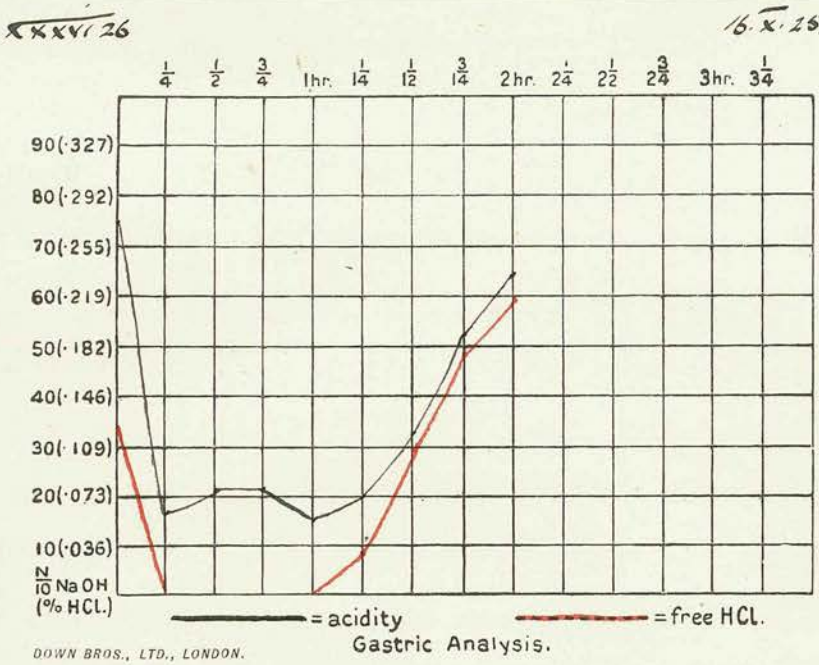
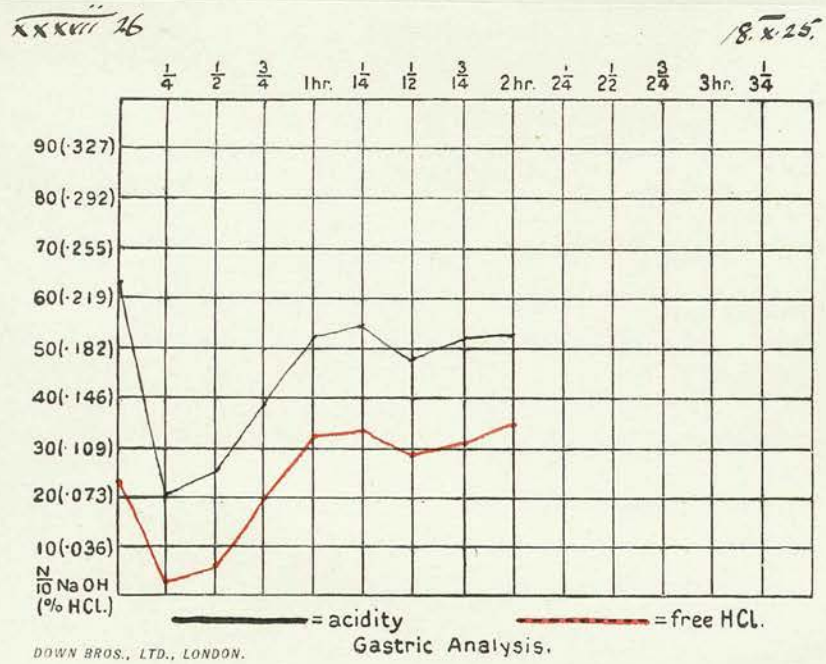


CHART IV.



patient had considerable difficulty in swallowing the tube.

CHART IV obtained on 18.X.25. When patient swallow the tube easily in comparison with the first test.

Had these patients been examined at a later stage during the present investigation I should have used the stilette method of introducing the tube, but I had not devised the stilette at the time when these patients were examined, and indeed it was the results obtained in these two cases that prompted me to find some method by which this distress, associated with the first test on some occasions might be alleviated.

The third case illustrated a gross difference between the results obtained from a subsequent test, but in this case the lower result was obtained from the second test meal, during which emotional stresses were practically non existent in comparison with those ruling during the first test. So that in this case at least a cause, other than emotional disturbance, must be sought for to account for the different results obtained.

CHARTS/

CHART V.

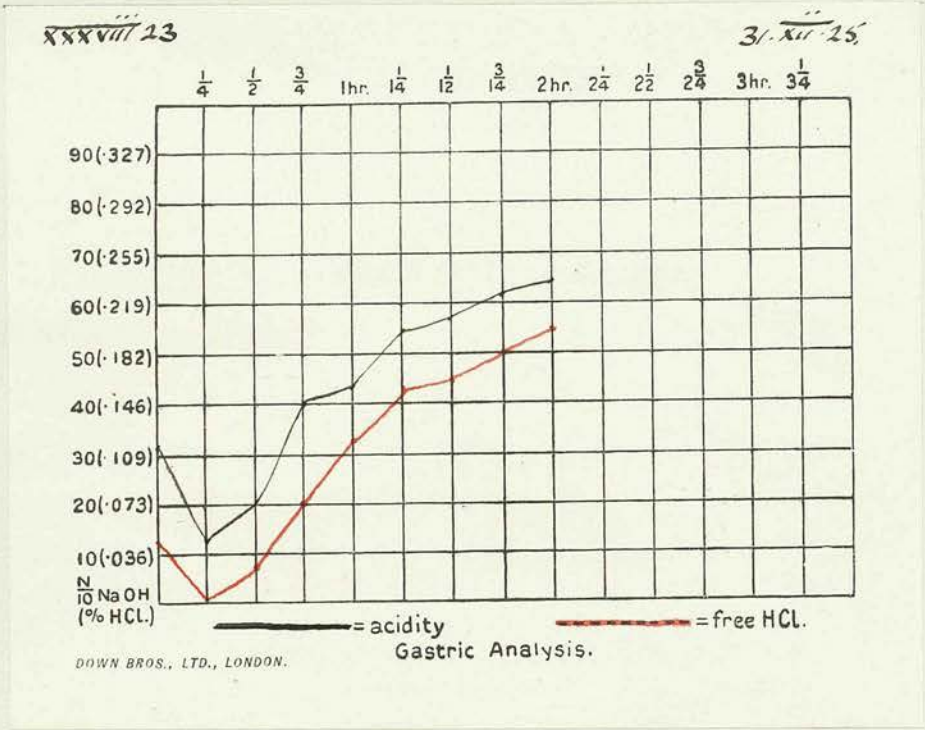
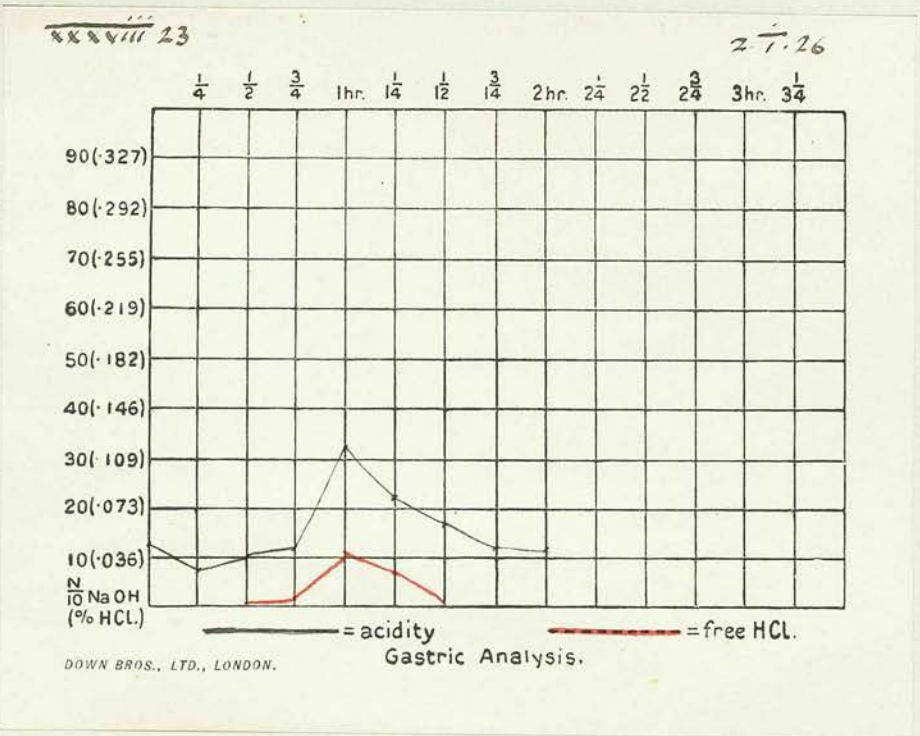


CHART VI.



VI

CHARTS V. & VI.

CASE (LXIV).

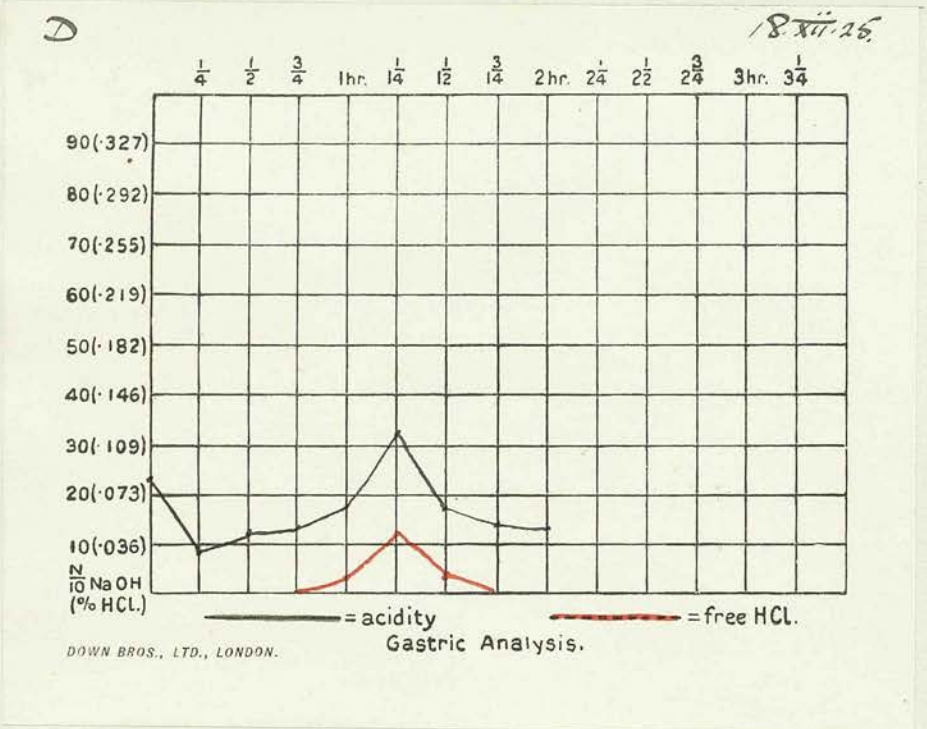
Male aged seventy two. Diagnosis:- Carcinoma of Stomach (confirmed by operation).

CHART V. obtained on 31.XII.25. When patient experienced rather more difficulty than is usually evinced at a first test, but his difficulty was not sufficient to suggest to me that the stilette should be used.

CHART VI. obtained on 2.I.26. When patient swallowed the tube easily.

There was one other case which I may mention in this connection, as suggestive of mental and physical distress accounting for variations in consecutive tests. This patient had no difficulty in swallowing the tube during either the first or the second test, but there was a marked diminution in the acid response obtained on the second occasion, and it transpired later that during the second test the patient was experiencing the slight pain and headache which always, with her, preceded menstruation/

CHART IX.


D
18.XII.25.
¼ ½ ¾ 1hr. 1¼ 1½ 1¾ 2hr. 2¼ 2½ 2¾ 3hr. 3¼
90(·327)
80(·292)
70(·255)
60(·219)
50(·182)
40(·146)
30(·109)
20(·073)
10(·036)
N/10 NaOH (% HCl.)
= acidity
= free HCl.
DOWN BROS., LTD., LONDON.
Gastric Analysis.

IX

CHART VII.

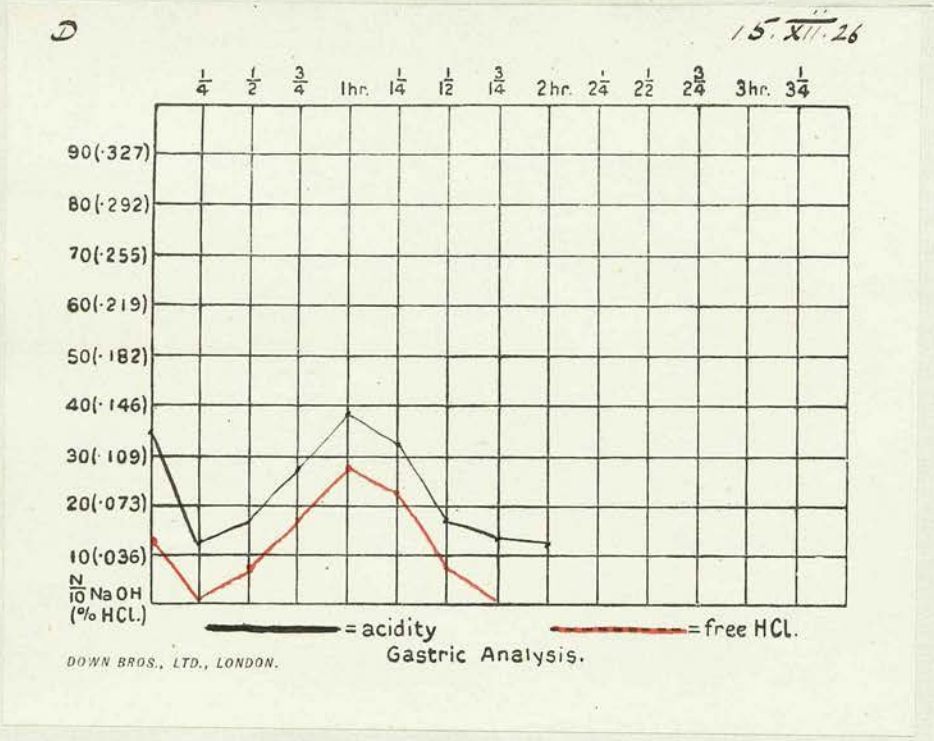
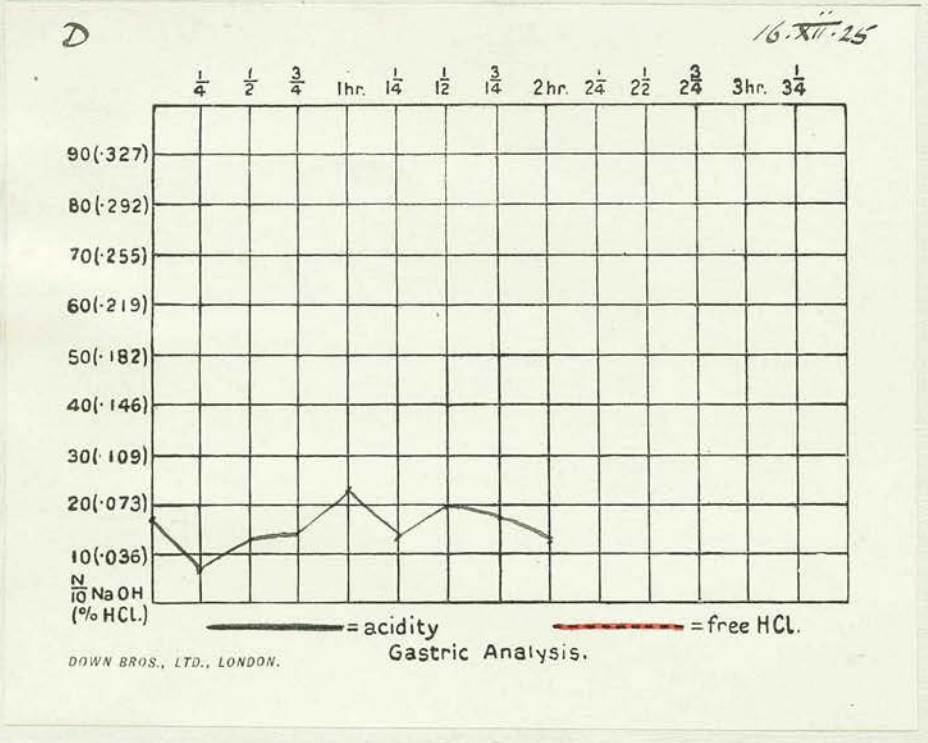


CHART VIII.



menstruation by a few hours.

CHARTS VII. VIII. & IX.

CASE (XVIII).

Female aged thirty two years. Diagnosis "Habit and Nervous Dyspepsia".

CHART VII. obtained on 15.XII.25. Tube swallowed easily.

CHART VIII. obtained on the following day, namely 16.XII.25. Tube swallowed easily. Menstruation commenced on this morning accompanied by premenstrual dysmenorrhoea.

CHART IX. obtained two days late, namely 18.XII.25. Tube swallowed easily. Menstruation still in progress, but unaccompanied by any upset at this stage.

In recording the results of their examination of one man by fractional analysis on twenty consecutive days. BELL & McADAM (16), lay some stress on the fact that the acid curve obtained on the first day was definitely lower than those obtained on the days that followed. It seems to be held generally that while the circumstances of the test are/

are unusual to the individual there is a tendency for inhibition of secretory response to occur, so that the indication of the acid state will err on the low side.

Examination of the results obtained in my series of cases does not support this view.

To investigate this point I have excluded all cases in which there was achlorhydria in both tests as affording extremely unreliable information in regard to gastric secretory response. I have considered only those cases in which Free HCl was present either on one or both occasions. Of such cases I have fifty seven.

Excluding the resting content the highest percentage of Free HCl registered on each chart has been taken to indicate the degree of response obtained on each occasion.

The results may summarised as follows:-

FIFTY SEVEN CASES - MALE & FEMALE.

Greater Response from 1st. Test	61.4%
Greater Response from 2nd. Test	38.6%

THIRTY THREE CASES - MALE.

Greater Response from 1st. Test	60.6%
Greater Response from 2nd Test	39.4%

TWENTY/

TWENTY FOUR CASES - FEMALE.

Greater Response from 1st. Test 62.5%

Greater Response from 2nd. Test 37.5%

It might be said with some justification that the use of the stilette, to which I have referred, would influence the results obtained in this respect, for the stilette was used on the occasion of first tests only. However the stilette was not devised till the present investigation was well under weigh.

On examining these fifty seven cases, to which I have just referred I find that the stilette was used in seven cases only, four female and three male. In these seven cases the first meal showed greater response in three instances, while in the other four the second meal showed greater response of HCl. Also I would repeat that the stilette is not used after the tube has been introduced some six inches, so that the difference which the stilette has made in the recorded cases is probably not significant.

The/

The limited numbers in this series of cases prohibits any significance being attached to the slight difference of percentage between male and female results, but there would seem to be definite indication from the above figures that the circumstances of a first test do not play any part as a general rule in inhibiting the secretory response.

(d) I have considered above certain inaccuracies in the stimulus, in so far as they may affect the acid state of the stomach for comparative purposes.

It must be made clear that if the test is considered as giving any indication of the comparative secretory responses by different stomachs to the same stimulus, then the varying rates at which the meal will leave different stomachs allows marked differences in the duration and fluctuations in the strength of stimulation, consequently the actual amount of the secretory response is influenced by these factors.

This point which is of considerable importance in the present study will be elaborated immediately.

THE ACID RESPONSE.

(a) In order to secure an accurate estimation of the gastric secretory response, as judged by the acid secretion of the stomach, the volume of juice secreted, together with its true percentage acidity would require to be known.

On theoretical grounds there are objections to the adequacy of even this data, for the limitation of percentage acidity (no higher figure than 0.6% having been recorded) allows of variations, in the direction of increase of fluid constituent of the juice, without a corresponding increase in the HCl output. Practically, however, stimulation of the stomach up to a maximum secretion must be extremely rare.

In the present test, however, the volume of juice secreted is diluted to an uncertain extent by food, saliva and regurgitated duodenal juices, and further an unknown amount of juice may be evacuated into the duodenum, while the real acidity is masked by neutralisation from food, saliva, duodenal regurgitation, and secretion from the pyloric antrum, so that/

that clearly accurate measure of the secretory response cannot be expected, and this test can be relied on only to show gross alterations in the secretory response.

The same objections do not hold when the test is being used as an estimation of the acid state of the stomach during the digestive phase, for those factors which militate against accurate estimation of secretory response, are at work under normal conditions in influencing the acid state of the stomach, and they play a definite part in the digestive phase itself.

Many observers BOLTON & GOODHART (17), BENNETT & RYLE (15), SPENCER, MEYER, REHFUSS & HAWK (18), have confirmed the fact that duodenal regurgitation is part of a normal sequence of events in the digestive cycle.

BOLTON & GOODHART (17), observe that duodenal regurgitation is not an intermittent leak into the digesting stomach in small amounts, but that at a definite point, as the stomach is emptying and the curve of acidity is rising, the pylorus relaxes and allows a considerable reflux of intestinal juices. This reflux/

reflux they find, rapidly brings down the acidity as the stomach empties, and determines the form of the curve.

BOLDYREFF (19), described this regurgitation as the important factor in the self regulating mechanism of gastric acidity which he demonstrated. He showed that pancreatic secretion was of primary importance, while saliva, bile, succus entericus, and pyloric antrum secretion were of very secondary importance.

So that fallacious (as judged by the normal standard for the particular stomach concerned) percentage of acidity might possibly be produced by anything causing abnormal regurgitation or to a less extent, excessive salivation.

The possibility of retching and an abnormal degree of salivation being produced by the circumstances of the test have been discussed already and described as infrequent. It will be realised that should it occur it may have more far reaching effects than merely alteration in the degree of stimulation by emotional disturbance.

It is only fair to state that LYON, BARETT & ELLINSON (20), record their belief that "frank macroscopic/

macroscopic regurgitation of bile into either a fasting or digesting stomach is an abnormal finding".

They find two exceptions to this rule, firstly in the case of patients in whom retching is produced, and secondly in certain cases of very marked hyperacidity, in which apparently, special provision is made for attempts to reduce the acidity by duodenal regurgitation.

The observations which they have made in support of their view are firstly, that in health in the fasting state the duodenum is free from bile, and secondly, that the normal direction of progression is always aboral, so that there should be no reverse peristalsis. They criticise other observers for considering that a series of medical students may really be considered as normal subjects, and remind them that the mere absence of presenting complaints does not mean that there is no disturbance of gastric physiology.

I shall add only, that if LYON, BARTLE & ELLINSON (20), are correct in their view then, from the experience gained in this series of cases. I must conclude that regurgitation of bile is to be regarded/

regarded as one of the earliest and most frequent manifestations of disordered gastric physiology and pathology.

(b) In order that the acidity curves obtained by fractional analysis, be of any value for comparative purposes the assumption must be made either that the gastric contents are a homogeneous mixture, or else that the samples are withdrawn relatively from the same part of each stomach.

Clearly if in each stomach the whole contents are thoroughly and efficiently mixed, then it matters not from what part the samples are withdrawn, but if the mixing is not thorough, or takes place only at some later period in the digestive phase, then the constitution of the samples depends entirely on the position of the tip of the tube in each case.

Unless the tip of the tube lies constantly relatively in the same position in different stomachs and in one stomach on different occasions, then the results obtained are of little use for comparative purposes.

Several observers have shown that apparently the constitution of the stomach contents varies at different levels, during the early stages of digestion/

digestion at least.

McLENDON (21), using his electrode for recording the H-ion concentration of gastric contents in situ, demonstrated by moving the electrode into different positions in the stomach that though stomach contents begin to mix at once after ingestion, yet it requires two or three hours before the mixing is thorough.

While GRUTZNER (22), by giving solid foods of different colours at varying intervals, found that this food remained in relatively undisturbed state for nearly an hour.

More recently GORHAM (23), challenged these workers who employed the fractional method of gastric analysis, for assuming that the gastric contents were a homogeneous mixture. He made the experiment repeatedly of withdrawing the gastric contents at the end of three quarters of an hour in 10 c.c. samples. He removed each sample as rapidly as possible, this usually occupied rather less than ten minutes, and he found very wide variations in the acidity of different samples.

WHEELON (24), in similar experiments, found that the acid concentration was far from constant in all/

all portions of the gastric contents at the end of one hour.

While KOPELOFF (25), repeated GORHAM'S experiments, and confirmed his results. Further in one case he introduced three tubes into the stomach at the same time, and allowed the tips to be at different distances from the teeth. The samples obtained from these tubes showed widely divergent curves of acidity.

WHITE (26), investigated very fully fifty cases from this point of view. He found that in 40% of these cases variations in acidity of from twenty to thirty points occurred in different samples of gastric contents, though these had been removed practically at the same moment.

The average difference amounted to seventeen points in the case of the Free HCl and twenty two points in the case of the Total Acidity.

He employed GORHAM'S technique in all his cases, but in addition he repeated his experiments in some of the cases, and studied the simultaneous variations to be found at other stages of the digestive phase. He concludes from these investigations that simultaneous variations are lowest in the fasting stomach/

stomach. Further the variations seemed to increase proportionately with the pouring out of acid, and were greatest between the periods of three quarters to one and a quarter hours following the meal, later in the digestive phase variations were generally less.

In a few experiments he tried to mix the stomach contents in situ artificially by alternate suction and compression of the syringe, and in these he found the average variations were reduced to ten points for Free HCl, and eight and a half points for Total Acidity at the end of the first hour period.

CARMICHAEL (27), informs me that he has found great variations in the samples obtained from two tubes passed into the stomach for the same disance, and in one case he obtained free acid in the samples withdrawn through one tube, while samples withdrawn at the same time from the other tube contained no free acid.

In the present series of cases I performed an experiment which has some bearing on this point.

On ten occasions I withdrew the tube one inch after the second, fourth, and sixth samples had been aspirated. After the tube had been withdrawn slightly in this way I aspirated a small sample from the new position.

The/

The tube was then swallowed again, as far as the original mark, and the whole process did not occupy more than a moment each time.

The results obtained are shown in the TABLE I. below:-

TABLE I.

	HALF HOUR				ONE HOUR				ONE & A HALF HOURS.			
	TUBE at PYLORIC MARK		TUBE ONE INCH OUT		TUBE at PYLORIC MARK		TUBE ONE INCH OUT		TUBE at PYLORIC MARK		TUBE ONE INCH OUT	
CHART	F.A.	T.A.	F.A.	T.A.	F.A.	T.A.	F.A.	T.A.	F.A.	T.A.	F.A.	T.A.
X.	--	22	10	28	22	32	14	36	20	40	24	46
XI.	--	18	--	16	--	18	--	20	--	22	--	24
XII.	14	32	14	34	28	36	28	42	26	40	28	44
XIII.	22	40	--	16	18	28	--	20	22	34	--	20
XIV.	26	38	20	30	--	14	--	12	--	16	--	8
XV.	10	20	28	42	34	46	36	48	44	54	44	58
XVI.	16	40	20	42	22	42	16	36	--	22	--	18
XVII.	--	20	--	16	30	48	28	50	38	54	36	50
XVIII.	4	16	--	42	12	50	16	44	6	14	4	16
XIX.	6	22	12	32	34	52	40	68	38	54	50	62
AVERAGE DIFFERENCE	F.A. = 7 T.A. = 10.6				F.A. = 4.6 T.A. = 5.4				F.A. = 4.4 T.A. = 5.6			
MAXIMUM DIFFERENCE in any case.	F.A. = 22: T.A. = 26				F.A. = 18: T.A. = 16				F.A. = 22: T.A. = 14			

F.A. = Free HCl. T.A. = Total Acidity.

The figures represent cubic centimetres of $\frac{N}{10}$ NaOH per hundred cubic centimetres of gastric contents.

My reason for choosing intervals of half an hour for the experiment in each case, was that I thought it possible that the gastric contents might gradually become a more homogeneous mixture as the digestive phase proceeded. And the results obtained are of some interest in this connection.

It will be noticed that the average difference of Free HCl found in these ten cases is very much more marked at the first half hour period than during the hour, or hour and a half period.

The figures for Total Acidity shew relatively the same results as those for Free Acidity.

And I would note here that these figures far exceed those which WHITE (26) considers fall within the margin of error, when care is taken in testing gastric samples.

The average difference is, perhaps, not so striking as the difference found in particular cases, e.g. Chart XIII. from a patient with a chronic gastric ulcer, causing pyloric obstruction (confirmed at operation), in which no Free HCl was found in the samples withdrawn when the tube had been taken out one inch, despite twenty-two, eighteen and twenty-two points respectively being recorded while the tube was/

CHART XVIII.

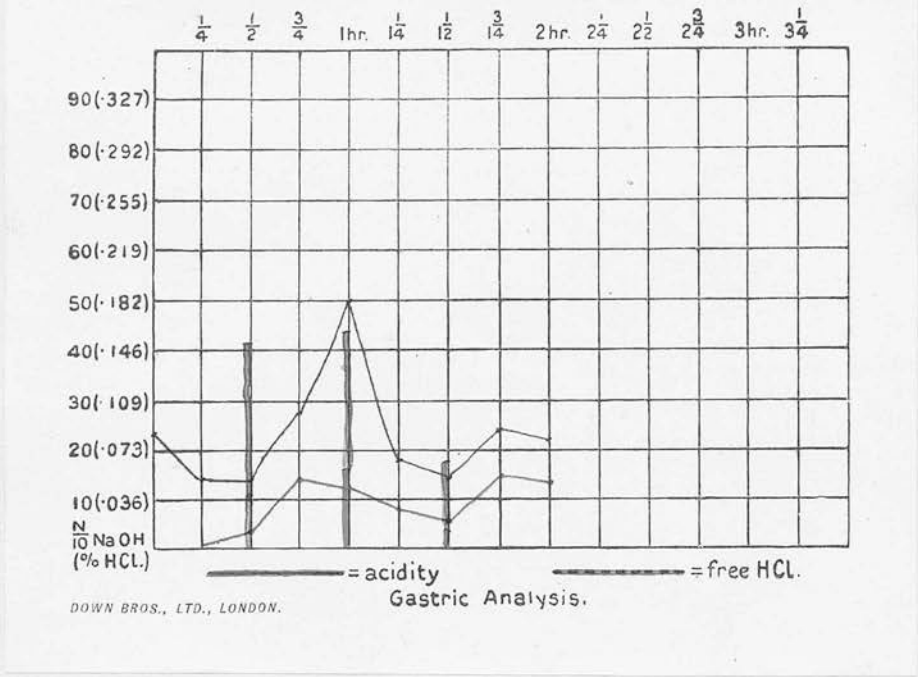


CHART XIX.

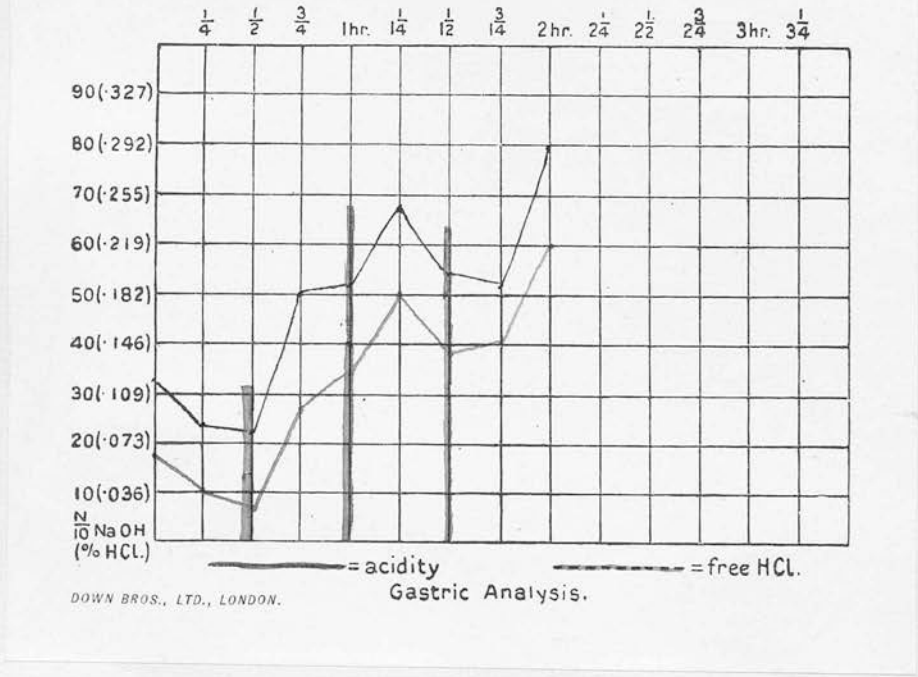


CHART XIV,

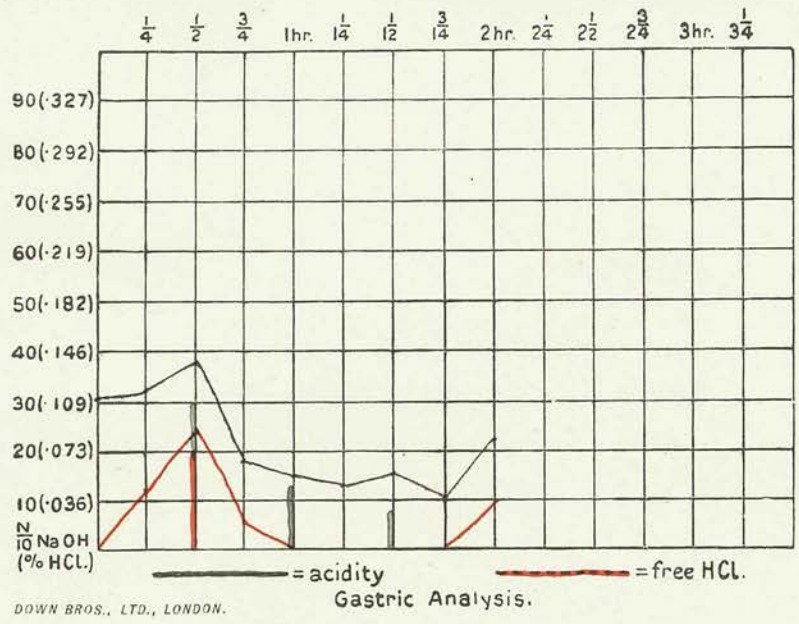


CHART XV.

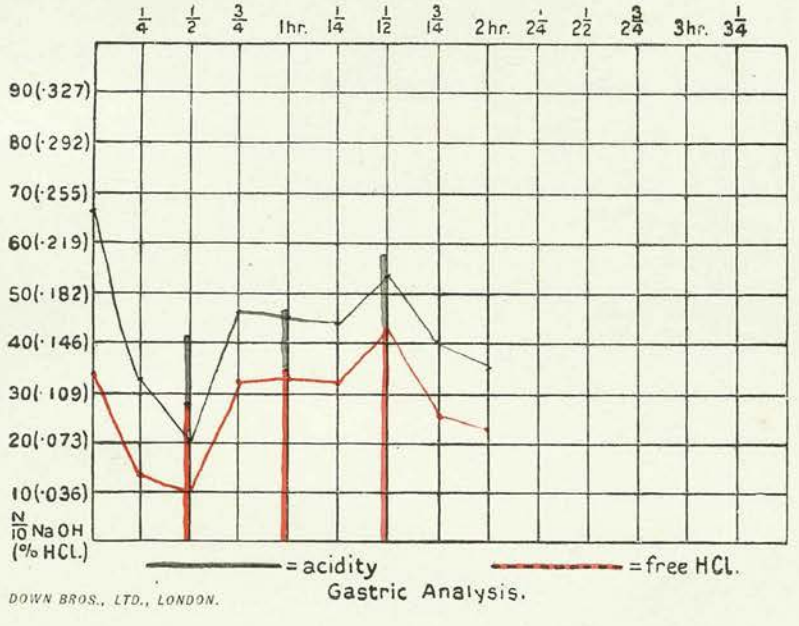


CHART XVI.

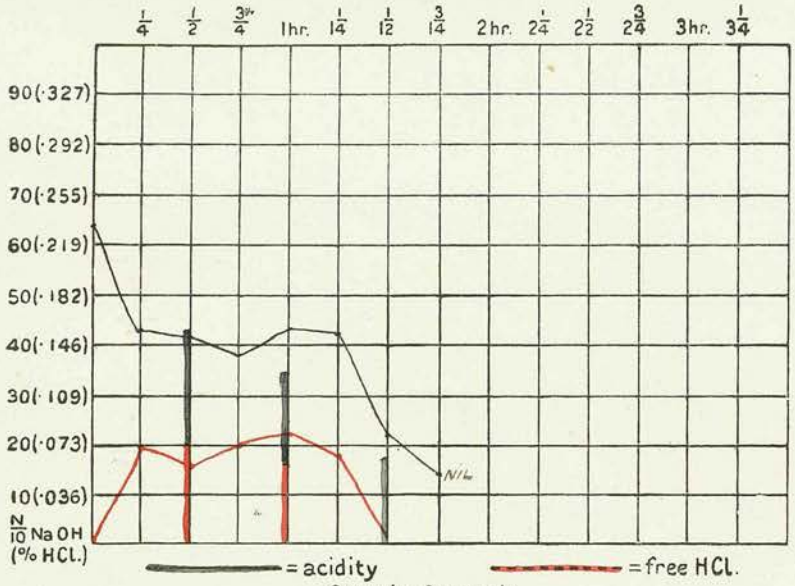


CHART XVII.

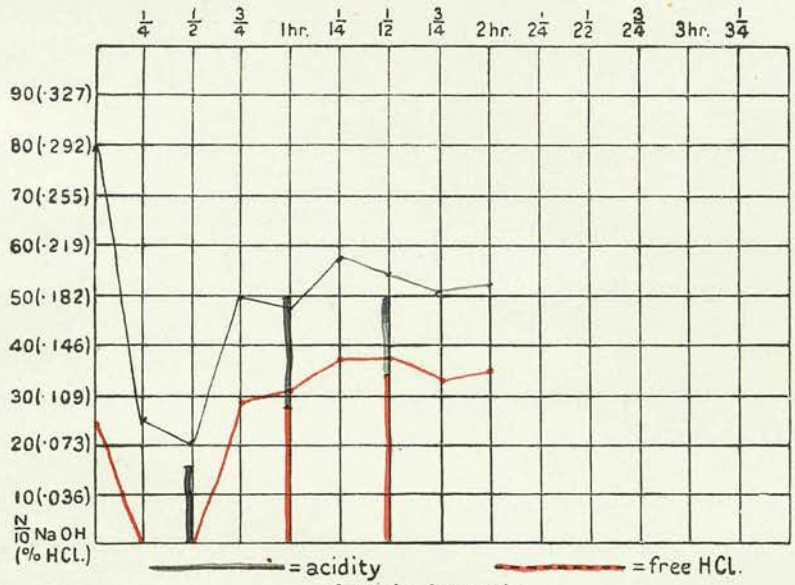


CHART XII.

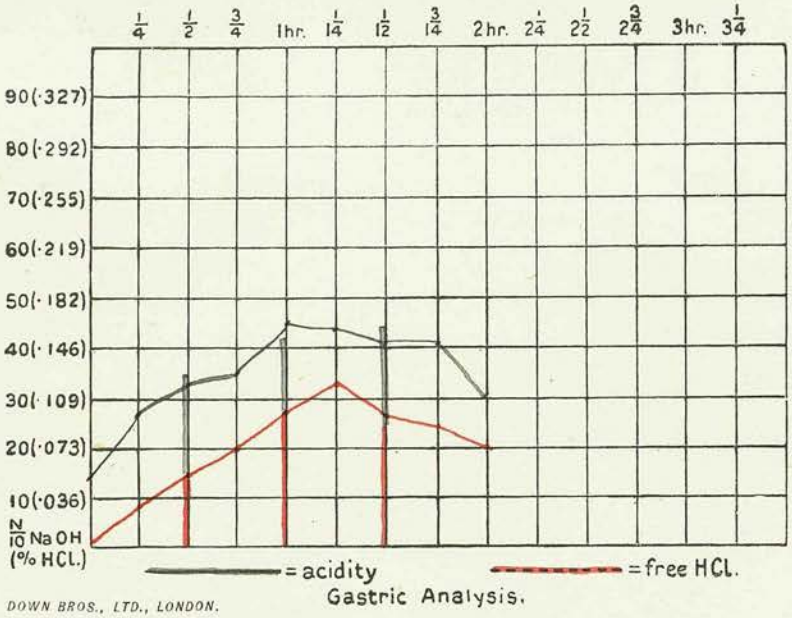


CHART XIII.

Chart XIII

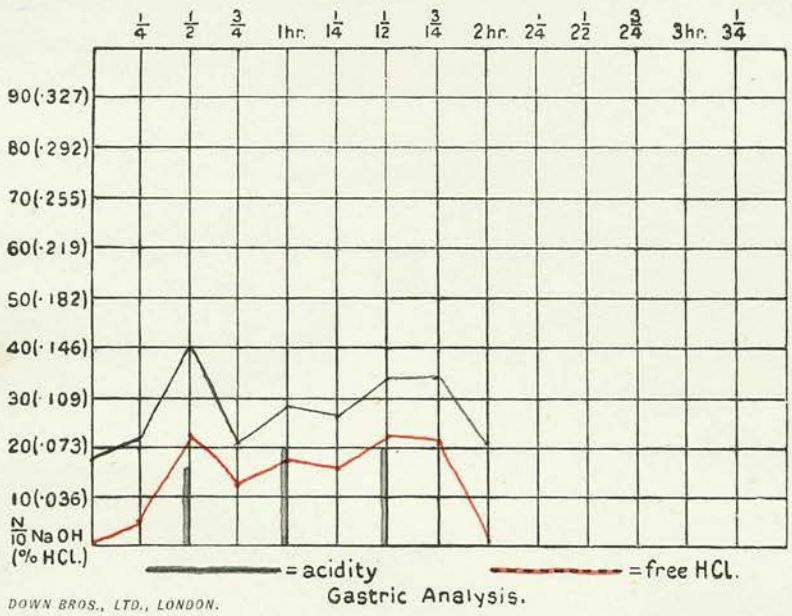


CHART X.

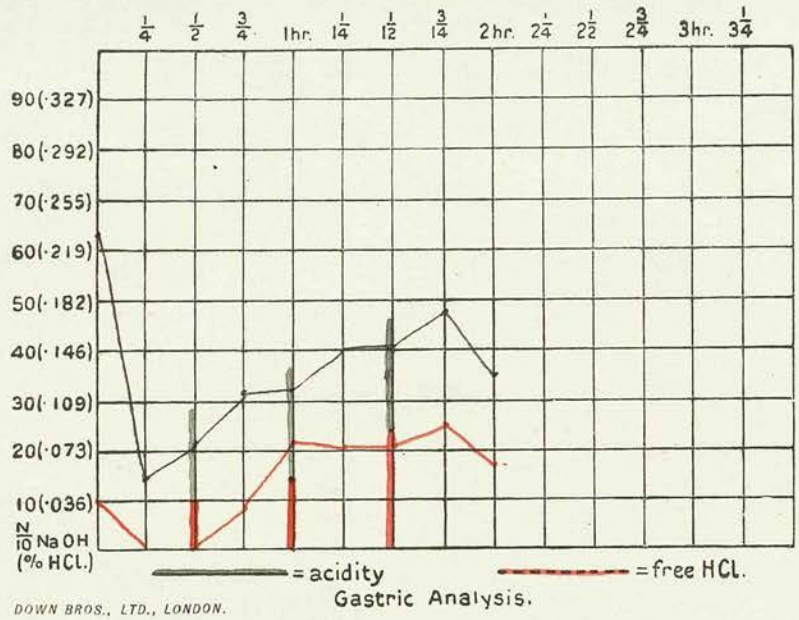
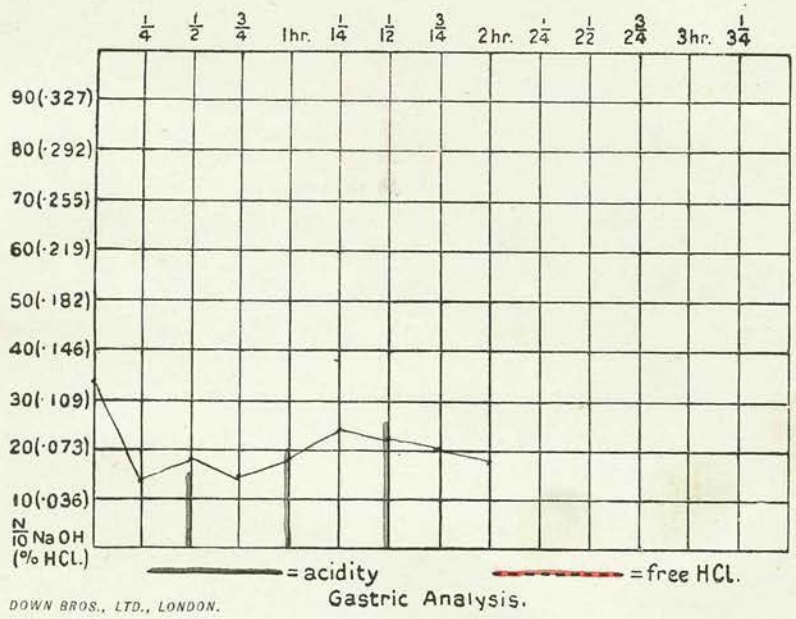


CHART XI.



was at the pyloric mark. These differences are, perhaps, more striking when shewn graphically. (CHARTS X. - XIX.)

In a further ten cases I repeated GORHAM'S EXPERIMENT: but it was at the end of two hours that I removed the whole contents as rapidly as possible.

These particular cases were selected because the amount of residue was very similar. Sample "8" was withdrawn in the usual way, and examined: the remainder of the contents was withdrawn as rapidly as possible (this did not take more than five minutes in any of these cases), mixed together and a 10c.c. sample taken for examination.

The Table below (Table II) shows the results obtained.

CHARTS X-XIX - The curves obtained while the tube remained at the pyloric mark are shewn in the ordinary way. The acidity of samples withdrawn at the half hour, one hour and one and a half hour periods is shown by a vertical line at these time periods.

TABLE II.

AMOUNT in cc.		42	50	38	25	35	35	40	35	45	35
SAMPLE 8	(F.A.	16	20	--	10	--	24	--	60	32	16
	(T.A.	34	30	20	22	10	36	12	72	46	36
AVERAGE of	(F.A.	17	22	--	4	--	30	—	56	22	16
RESIDUE	(T.A.	38	32	19	18	14	38	8	66	32	34

AVERAGE DIFFERENCES:- F.A. = 2.8: T.A. = 3.9

MAXIMUM DIFFERENCE in any case:- F.A. = 10: T.A. = 14

F.A. = Free HCl. T.A. = Total Acidity

The figures represent cubic centimetres of $\frac{N}{10}$ NaOH per hundred cubic centimetres of gastric contents.

These results certainly show a smaller average difference than that recorded by GORHAM, whose experiments were performed at the end of three quarters of an hour of digestion. And bear out the view that the contents only become a homogeneous mixture late in the digestive phase.

Though the experimental results shown in Table II. are not quite comparable to those in Table I, yet they are suggestive of a steady mixing process continuing even after the first one and a half hours of the digestive phase. For while the average difference of Free HCl recorded at the end of an hour and a half is 4.4, this figure has been reduced to 2.8, as indicated by the results, shewn in Table II.

The/

The fact that the fractional method of gastric analysis is still viewed with favour in many quarters, presumes a satisfactory answer to this criticism. Yet so far as I can find none has ever been given.

BOLTON (28), replying to criticism along these lines, at the British Medical Association Sectional discussion upon "Modern Methods of Stomach Investigation", is reported as saying merely that the churning action of stomach movements must ensure thorough mixing.

BENNETT (29), writes "These criticisms depend chiefly on gastric contents not being homogeneous, and if a small quantity is removed and analysed it cannot be expected accurately to represent the contents as a whole.

There is a measure of truth in this, but the criticism loses force if care is taken to remove a large specimen from time to time and it must further be recognised that any method such as a fractional one in which the whole contents of the fasting stomach are removed before the test meal is given must be far more accurate than the ordinary EWALD technique/

technique, in which at the end of one hour a mixture of meal with old and recent secretion is removed and examined without the observer having any information as to what was in the stomach to begin with".

(I presume "a large specimen from time to time" corresponds to 12 c.c. at intervals of quarter of an hour which is the technique he describes later).

Answering GORHAM'S challenge RYLE (11), writes "having regard for the fluidity of the gruel meal, and the constant activity of the stomach during digestion, it is difficult to believe that the contents can escape thorough mixing.

On studying the reports of GORHAM and KOPELOFF it appears that they did not employ the gruel meal. KOPELOFF employed the tea and toast meal, and GORHAM shredded wheat and water.

With meals of this nature it is obvious that a certain amount of sedimentation will be liable to occur; that the farinaceous portions will be mixed with saliva; and that there will be greater variability in the fluidity of the samples.

The experiments of GORHAM and KOPELOFF thus require repetition with the gruel meal. Even allowing that their criticism may be reasonable from the/

the scientific standpoint, it need not be held to invalidate the practical utility of the test.

WHEELON supports GORHAM'S findings, but does not condemn the clinical employment of the test meal.

Fractional analysis is chiefly employed as a clinical test and can never by any stretch of imagination be regarded as an accurate chemical procedure. It must be clearly appreciated that its findings merely portray in a general way the results of the numerous processes influencing the chemistry of the gastric contents from moment to moment".

It would appear to me, however, from a study of the observations of several workers, that there is strong reason to doubt whether the gastric contents are mixed uniformly during the first hour of digestion at least.

Should this prove to be the case then the value of the test meal may possibly lie rather in the fact that all the samples are drawn from more or less the same position throughout all tests.

I have quoted RYLE at some length in this connection, for, while agreeing with him that the experiments/

experiments of KOPELOFF and GORHAM " need not be held to invalidate the practical utility of the test", I consider his defence inadequate in this connection.

From my own observations and from a study of the literature available. I cannot subscribe to his statement that "it is difficult to believe that the stomach contents can escape thorough mixing".

Nor do I find the answers which BOLTON and BENNETT have made in face of this criticism satisfactory. I have indicated that a considerable amount of experimental evidence has accumulated which suggests strongly that stomach contents do not mix so rapidly, or so completely as is commonly supposed.

Certainly the evidence would seem to be worthy of a re-investigation of the "churning" action of the stomach, rather than a reiteration of an assumption for which no reference is given.

From the quotation of RYLE, which I have just recorded he would appear to suggest that the gruel test meal is a sine qua non for the fractional method of gastric analysis, and if he is right in hinting that accurate results can be obtained only by the use of a test meal of this consistency then this fact/

fact should be known more generally, and should be recorded as an essential feature of fractional analysis.

That this is not recognised by all observers is shown by the following quotation from MACLEAN (59), "The usual test meal employed is prepared by the adding of two table-spoonfuls of finely ground oatmeal to about a quart of water and boiling until the contents are reduced to one pint. The mixture is then strained through muslin when it is ready for use. The meal is very easily aspirated and does not tend to block the perforations of the tube.

The usual EWALD test meal of bread and tea may be taken instead of this gruel; it is perhaps more palatable but has the disadvantage that it frequently blocks the tube".

Theoretically the tip of the tube remains applied to the lowest part of the stomach in each case. For the fact that the site of the tip depends in principle, in each case on gravity, has been referred to already, and it is part of the technique that the tube be maintained in the same position throughout the test.

I believe that any constancy or merit for comparative purposes, which fractional analysis may show/

show, will be found to depend rather on this factor (the relatively fixed site of the tip of the tube than on a supposedly uniform mixture of gastric contents).

It is true that GORHAM (23), without being able to supply any corroborative evidence, has suggested that the position of the tip changes constantly with changes in the size and position of the stomach, by aspiration, by shortening and lengthening contractions, and by peristaltic waves tending to carry the tip towards the pylorus.

WHITE (26), in his experiments paid special attention to the position and movements of the tube tip by means of X-Ray examinations and screening during the course of the test.

He found that in 95% of his cases the tip of the tube "lay like a sinker on the lowest point of the greater curvature of the stomach, in the median line, or just to the right or left of it, and did not move a half inch in position during the withdrawal of samples".

The tip he concludes is not moved much at all by peristaltic waves, and does not shift to different portions of the stomach.

I/

I find the evidence against a homogeneous mixing of stomach contents much more convincing than the evidence against continuous alterations in the site of the tube tip.

Even if it is allowed, however, that the tip remains more or less in the same position throughout each test, it is clear that there may be considerable differences in the site at which the tube rests in different stomachs. The distance between the teeth and the lowest level of the stomach will vary in each case, and can only be gauged roughly.

Possibly considerable error in this direction is permissible, however, since a relatively large area of the mucous membrane suggests histologically, the same degree of secreting capacity, and the action of gravity will always tend to bring the tip of the tube into contact with the mucous membrane.

Enough has been said to show that the test is open to adverse criticism on this score, while the fact remains that the test may not be condemned completely on theoretical grounds alone, if satisfactory practical results are obtained from it.

(c) Certain points in relation to the laboratory/

laboratory technique now remain to be considered.

(1) In my own cases the test meals were examined in every instance within twelve hours of the test.

MAURIN (30), recorded finding a gradual increase in acidity for forty eight hours following the withdrawal of samples, and while the contents were still in test tubes at room temperature.

He found that the rise in acidity varied from .2% to .3% in forty eight hours, after which it diminished again gradually.

BARTLE & MALGOYRE (31), were unable to confirm MAURIN'S results, and found that there was a tendency for the acidity to fall. Their observation receives certain support from MATTHEWS (32), who showed that in prolonged peptic digestion there is a steady increase in the power of combining with acid as is shewn by the steady fall in the amount of free HCl.

LYON, BARTLE & ELLINSON (20), consider that the samples should be examined immediately after withdrawal if possible, and give as their reasons that evaporation increases the acidity of the material, while the continuation of digestion changes the relation/

relation of Free HCl and Total Acidity.

In six cases I retested samples which had been left standing at room temperature, with the ends of the tubes closed by a plug of cotton wool, for another twenty four hours after the first test.

The differences in the results were slight in all cases, and no more than could be accounted for by experimental error, when it is considered that any trace of error either in measuring the 5 c.c. sample, or in reading the burette (which gives tenths of a cubic centimetre of $\frac{N}{10}$ NaOH readings only) is multiplied twenty times before results are charted.

Even with excessive care WHITE (26), finds it impossible to avoid errors of two or three points of percentage in re-testing samples.

In the re-examination of these six test meals fifty four samples were re-tested. The maximum difference recorded amounted to four cubic centimetres of $\frac{N}{10}$ NaOH per hundred cubic centimetres of gastric contents. This difference was found in two samples only.

The other samples either showed no difference on re-examination, or else the difference found fell/

fell within the scope of what WHITE considers an unavoidable error. So that it would seem there is little or no significance to be attached to the duration between the collection and the testing of the samples.

The only observation worthy of record in this connection was in the case of a patient who had had a partial gastrectomy and gastro-duodenostomy performed, and the samples were heavily tinged with bile throughout.

When tested on the second occasion the bile pigment had settled to the bottom of the tube, and I was able to detect the presence of Free HCl in two tubes, which on the occasion of the first testing had seemed to me to contain no trace of Free HCl as judged by TOPFER'S reagent, despite particular attention which I had paid to the colour change with a view to observing the first trace of Free HCl in this somewhat unusual case. But I regret having to record that the GUNZBERG test was not performed in this instance.

(2) There are certain observers who have objected/

objected to the particular technique of acid estimation which is employed most generally(and which I have adopted in my cases) as being inaccurate.

With regard to acidity the samples are tested for Free HCl and Total Acidity so-called.

The Free HCl is regarded as being that part of the HCl which is not combined with protein or any other potential base. While the Total Acidity is regarded as being due to different factors in varying degree - namely, to Free HCl, to organic acids, to acid salts, to HCl combined with protein (or protein salts of HCl as HAWK (33) prefers to call it) and to a slight extent to Carbon,Dioxide. (BENNETT & RYLE (15)).

That titration with standard alkali using phenolphthaleim as an indicator, can indicate Total Acidity with sufficient accuracy seems undisputed.

COLE & AIDIE (34), however, do not find in TOPFER'S reagent a sufficiently accurate indication of Free HCl. They observe that its range of indication allows anomalous results to be given, for it first indicates the neutralisation of Free HCl only, but later when the major part of the Free HCl has been/

been neutralised, it indicates some neutralisation of protein salts of HCl as well.

They recommend the use of the Thymol Blue indicator of CLARK & LUBS[35], as giving a more accurate range of indication. This, however, is very much more tedious to use than TOPFER'S reagent, for it requires colour changes to be matched with standard acids.

KOPELOFF[25], supports this contention, and advises estimation of acidity by H-ion concentration and buffer salts.

Many observers (LANZ[36], McLENDON[21], KALK & KUGELMANN[37], NOGAAD[38]), who have conducted tests upon the comparative value of different methods, agree that inaccuracy occurs to any appreciable extent only when the protein constituent of gastric contents is high, while they nearly all find that the H-ion concentration is the most efficient method of estimating acidity.

COLE and AIDIE allow that the difference between H-ion concentration and Free HCl as shown by indicators is practically negligible when the acidity is at all high, or when the gastric samples contain little/

little protein. (And I would note here that the quantity of protein in the gruel meal about 5 grams - can hardly be regarded as producing a high protein content).

A further objection that the action of TOPFER'S reagent is affected by the presence of organic acids is refuted by RUFFELL (39). As the result of careful investigation he concludes that organic acids, produced by the Oppler Boas bacillus, or by acid streptococci, never attain, in the stomach, an acidity great enough to affect TOPFER'S reagent.

MATTHEWS (32), supports this contention, and finds that any organic acid occurring in the stomach, would require to be present in a concentration of at least .5% before it would affect this indicator.

In the present series of cases, however, I have observed the custom of confirming a reaction to TOPFER'S indicator by GUNZBERG'S test in all cases in which Free HCl appeared to be present in traces only, or in which the presence of the Free HCl had not been anticipated in view of the clinical condition.

In all such cases I found that the indication afforded by TOPFER'S reagent was confirmed by the/

the GUNZBERG test.

(3) It will be convenient to consider in greater detail, at this stage the relationship which these two acidities, namely Free HCl and Total Acidity bear to the HCl secreted.

The HCl secreted is distributed between the protein salts of HCl, neutralised HCl, and as a general rule there is left a certain amount of Free HCl.

It is clear that neither the curve of Free HCl, nor the curve of Total Acidity, which includes dependency on other factors than the HCl produced, truly represent the curve of the entire HCl secreted.

The problem may be approached from another aspect, however, by using the estimation of the Chloride radicle. BOLTON & GOODHART (17), have conducted a series of estimations of the chlorides by VOLKARD'S method (unfortunately a tedious and elaborate procedure), in samples from fractional analysis, and they have obtained curves of Total Chloride, Inorganic Chloride, and Active HCl in this way.

This active HCl is represented by Free HCl and protein salts of HCl, but does not depend in any way/

way upon the neutralised HCl, so that the curve does not represent the total HCl secreted. While the curve of Inorganic Chlorides includes the neutralised HCl as a partial factor only.

These observers find, however, that the curve of Total Chlorides most nearly represents the curve of HCl secretion. (Apart from HCl the chlorine in other digestive juices does not amount to more than.....0.1%.)

When this curve is rising the stomach is secreting chloride, while when a fall takes place in the curve the indication is that a fluid containing less chloride than is present in the gastric contents, e.g. duodenal regurgitation is diluting these contents.

For most practical purposes the curves of Free HCl and Total Acidity form as satisfactory an indication of gastric secretion as can be obtained from the samples. When the acidity is low, or free HCl is absent entirely it cannot be assumed that these low curves alone indicate a diminished gastric secretion, for free or excessive neutralisation may account for this low acidity.

(As/

(As a rule the probability of free neutralisation will be shown by the presence of bile from duodenal regurgitation in the samples. But that duodenal regurgitation may have occurred without any indication from the presence of bile will be shown later).

It is in such cases, with low acidity, that estimation of the Total Chlorides can differentiate between poor secretion, and excessive neutralisation.

It may be noted in this connection that when chloride estimation has shown a low total acid curve to be due to absence of secretion rather than excessive neutralisation, it is difficult to explain the titratable acidity.

LIM (40), has suggested that the colloid nature of mucus play some part possibly by absorption of the alkali used in the titration. Some support is given to this view by the observations of BENNETT & RYLE (15), in connection with the differences recorded between the curves of Free HCl and Total Acidity.

These observers noted that in most cases the two curves were parallel, the Total Acid curve being at a level of about 10% NaOH above the Free HCl curve/

curve. But in cases with abundant secretion of mucus they noted that the difference amounted to about 18% NaOH. Some confirmation of this observation will be found when the Average Difference of Total Acidity in 'Difficult' cases is considered in the next section.

(d)

(d) The part played by Sex and Age in influencing gastric secretion is subject to considerable controversy.

(1) There seems to be no record of any extensive series of test meals in normal women, comparable to the well known series of normal men whom BENNETT RYLE (15), examined by fractional analysis.

Such observations as have been made are of doubtful value, since uniformity of technique is lacking.

For example KOPELOFF (41), records his results from fractional analysis in ten normal women, and by comparison the average response obtained seems rather greater than that in BENNETT and RYLE'S series of men. But as RYLE (11), points out the test meal used was different and possibly formed a more potent stimulus.

In a more extensive series of normal women (sixty seven) FOWLER & ZENTMIRE (42), investigated the resting juice only. They found that on the average their results differed in no way from those obtained by FOWLER, REHFUSS & HAWK (43), who had made similar investigations in an even larger series of normal males.

With/

With a view to discovering any sex difference in secretion NIKKI (44), examined a large number of healthy adults (Japanese) and found a slightly higher acidity in males, but he made his examination by the one-hour test meal only.

While WRIGHT (45), who also used the one-hour test found no difference between the sexes in two hundred and fifty school children.

CARLSON (3), however, considers it established that achylia, and possibly hypoacidity is relatively more common in women than in men. This is supported by BELL'S (46) analysis of four hundred and twenty five fractional test meals (the cases all being pathological), in which he found that women preponderate over men in the low curves in the proportion of 68.4 to 42, and men over women in the high curves in the proportion of 100 to 61.2.

He goes so far as to suggest that moderate degrees of hyperchlorhydria in women are much more noteworthy than similar degrees in men.

(2) WRIGHT'S (45), examination of two hundred and fifty school children between the ages of six and fifteen years, has just been referred to. He found on the average that his figures were similar to those from/

from adults.

It is generally held that such factors as grief, mental depression, anxiety, physical or nervous exhaustion, and pain have a definite inhibitory effect upon gastric secretion (I quote from RUSSELL (47)). There is, therefore, a natural tendency to assume that gastric secretion tends to be diminished with age.

HANEBORG (48), investigating the effects of alcohol upon digestion, noted that he found a tendency for gastric secretion to become less with age.

This is further confirmed by DEDICHEN (49), who examined the gastric contents of one hundred apparently healthy persons, between the ages of sixty-seven and ninety two years. He found that four fifths of the men, and three fifths of the women, showed achlorhydria, and that hyperacidity at this age period was very rare.

BELL'S (46), observations in his large series of pathological cases, to which I have referred already, are of interest in this connection.

He divided each type of curve into its decade incidence, and found that relative to the decade incidence of other types of curve, hyperchlorhydria/

hyperchlorhydria was very much more common after the middle decade (41 - 50).

II. STARCH.

The starch constituent of the test meal which has been given may be used conveniently in estimating the emptying of the stomach.

The presence of starch in any of the samples aspirated, may be shown easily and efficiently by the addition of a few drops of Iodine. The violet blue reaction given in the presence of starch is very definite, and could not be readily mistaken.

With the standard gruel meal as used in my series of cases, the earlier specimens do not require to be tested, for the deposit at the bottom of the tube shows clearly that food is still present. In the later specimens the food deposit becomes defined less clearly, and testing for starch is of definite value.

Of the whole technique of fractional test meals the starch test, as a guide to the emptying of the stomach, would appear to be open to the least criticism./

criticism.

If the resting contents of the stomach have been removed entirely, a starch-iodine reaction can be due only to the starch ingested with the test meal. While even if it be granted that complete removal of resting juice may not be achieved in every case, and that therefore, the stomach may contain starch from a previous meal, yet in such a case the indication of gross delay in emptying is given.

It must be allowed too, that in some cases, it is difficult to decide whether the minute flecks of violet blue, sometimes seen in very late specimens are worth recording as an indication that the stomach has not emptied itself. But for practical purposes, an error of quarter of an hour is immaterial.

With the standard gruel meal, BAIRD, CAMPBELL & HEIN (50), give the following table of the rate of emptying of the stomach, as judged by the starch test in one hundred and fifty seven normal males.

TABLE/

TABLE

RATE of EMPTYING of the GRUEL MEAL.

AVERAGE TIME of EMPTY-ING	1 HR. or BEFORE	STOMACH CONTAINS NO STARCH AT:-						
		1¼ hr.	1½ hr.	1¾ hr.	2 hr.	2¼ hr.	2½ hr.	2¾ hr. or later
2 hrs.	5.5%	4%	9.5%	12%	17%	15%	15%	22%

From this RYLE (11), notes that in health the extreme variations from the average normal time are not more than 50% of that time. He finds the rate of emptying the most constant and accurate of all the findings with the fractional test.

The remarkable constancy of the rate of emptying is shown from the results of BELL & McADAM'S (16) observations in examining the same man by fractional test meals on twenty consecutive days.

The observations which I have made in this connection, as a result of my investigation will be recorded in full in the next section. But I may note here that the rate of emptying is not so universally constant as the results obtained by BELL & McADAM from their single case, would suggest. In 35% of cases I have found an inconstancy which may be of some practical significance.

III. CHARCOAL.

In my series of cases I followed BENNETT'S (51) technique, and gave the patients charcoal powder in milk several hours prior to the test.

On the average the charcoal was given seven hours before the test meal, but a natural desire to refrain from waking patients merely for the purpose of giving the charcoal allowed all variations between six and eight hours before the test to be made.

The object of giving the charcoal is that it is a substance which can be recognised readily in the gastric contents, and when found in the resting contents should indicate gross delay.

BENNETT writes:-

"My personal practice is "to tell the patient to take a glass of milk contain- "ing two teaspoonfuls of charcoal on the evening be- "fore examination", and later adds "the presence of "charcoal, known to have been taken twelve hours prev- "iously, is always pathological".

Theoretically there would seem to be no fault to find with the above statement. In my experience/

experience, the only other substance with which charcoal in the gastric samples might conceivably be confused, is the dirty grey swallowed sputum such as is seen in miners.

(In one case XVIII the resting contents showed the presence of what I took to be charcoal at first, but further observation showed that the charcoal was all collected with a frothy deposit at the top of the specimen, whereas charcoal from the stomach collects in a deposit at the bottom of the sample.)

I have found no other reference to the use of charcoal in conjuction with the fractional test, than that which I have quoted above, and I can record only my own experience in these frankly abnormal cases.

In my series of seventy-five cases, I have found charcoal present in some degree, in the resting juice of one or other test in twenty-two cases.

It has been my experience, however, that charcoal may be found in the resting juice in amounts which vary considerably in degree.

Thus, in some cases a very definite heavy deposit of charcoal will be found, leaving no doubt as to the indication of gross delay. But in other cases, what may be called traces of charcoal are found These traces of charcoal are found usually in the form of particles intermingled with the resting con-

tents/

contents, and not formed into a deposit, but I have found all degrees of charcoal, present, from a few particles scattered through the contents up to a slight deposit, and so to a heavy definite deposit.

The inference to be drawn from scattered particles and slight deposits is not clear. Of the twenty-two cases, in which charcoal was found, nine have been cases in which there was a heavy deposit in both tests, and of these eight have been shown at operation to have organic lesions sufficient to account for gross delay, while the ninth showed evidence of gross delay in emptying clinically and by X-Ray, but operation was refused.

In no case have I found a heavy deposit of charcoal in the resting content of one test without a heavy deposit being found at a subsequent test.

In one case a slight deposit of charcoal has been found in both tests; but Clinical and X-Ray examination revealed no suggestion of delay in emptying, and at operation a duodenal ulcer insufficient to account for gross changes of function, was discovered.

Seven cases showed charcoal, noted as "traces" and certainly not comparable in quantity to a definite deposit, in both tests. In two of these cases/

cases clinical and X-Ray examination suggested no delay, in other two clinically, there was a suggestion of delay, but X-Ray examination did not confirm this; in one both clinical examination and X-Ray investigation suggested delay: while in the other two remaining, operation confirmed an organic involvement of the pylorus, which had been suspected by clinical and X-Ray examination.

Five cases showed charcoal in the resting content of one test only, in amounts noted as 'traces' In three of these cases investigation by other means showed no evidence of delay; in one operation revealed no evidence of pyloric obstruction: and in one both clinical and X-Ray examination showed marked evidence of gross delay.

It will be observed, therefore, that apart from a heavy definite deposit of charcoal in the resting content, the significance of charcoal present in other degrees has been uncertain. Further in some cases it is difficult to explain the absence of a heavy deposit of charcoal.

It is difficult to explain these apparently inaccurate indications which charcoal affords, as to the delay in emptying. But it is my impression, that 'traces' only of charcoal in the resting content are almost always associated with an unusual amount of mucus/

mucus. I suggest, therefore, that when charcoal is given in powdered form, there is a tendency for particles of it to adhere to the mucous membrane entangles in mucus, and that these particles stay in the stomach long after food given at the same time has left it.

I have been interested to note that RYLE who has collaboratee closely with BENNETT, in connection with the Fractional Method of Gastric Analysis, makes no mention in a recent, detailed account of the technique, of charcoal as an adjunct to the value of the test.

NOTE.

In the paragraphs which follow, consideration of my own cases, in connection with the subject matter dealt with, will be deferred until these subjects are considered along with an analysis of the Charts obtained from my cases.

IV./

IV. BILE.

The presence of bile in the samples can be detected with sufficient accuracy visually.

Its presence in gastric contents, as part of a physiological process, has already been referred to.

BENNETT (51), finds that bile regurgitates readily in normal people, and is usually present in later specimens, indeed, its absence is somewhat suspicious of an abnormal pylorus.

SPENCER, MEYER, REHFUSS & HAWK (18), have shown, however, that bile is a somewhat inconstant indication of duodenal regurgitation, for it sometimes happens that the presence of trypsin can be shown in gastric contents, in which there is no trace of bile, though they found that as a rule the higher the tryptic content the more deeply were the specimens stained by bile.

Further there seems some reason to doubt that bile in the samples is always due to physiological regurgitation. For BENNETT & RYLE (15), have observed that it is possible to withdraw a clear apparently/

apparently gastric specimen, and in the next syringeful, or in the second half of the same syringeful to withdraw bile stained fluid. They consider that under certain conditions suction at the tube tip may be produce an artificial reflux of bile.

(I have referred already to LYON, BARTLE & ELLINSON'S (20), statement that regurgitation of bile is not a physiological process, and lest it be thought that this artificial reflux of bile noted by BENNET and RYLE adds support to their view, I have thought it advisable to record that the technique of aspiration used by these two sets of observers appears to have been entirely similar).

V. MUCUS.

The presence of mucus to any marked extent in any of the samples is shown readily by the behaviour of the specimens while they are being aspirated, and while they are being manipulated for test purposes.

There is unfortunately no satisfactory method of estimating mucus quantitatively, and its amount can only be gauged roughly.

The origin of this mucus has been referred

to/

to already, while considering gastric secretion as a whole. In addition to gastric mucus, oesophageal secretion and mucus from other parts of the superalimentary and respiratory tracts, may also find their way into the stomach.

While any accurate investigation of gastric mucus remains difficult or impossible, the significance to be attached to varying degrees of mucus content lacks any precision.

RYLE (11), notes that mucus is generally more plentiful towards the end of the meal, and regards it as representing the protective alkaline secretion of the pyloric mucous membrane. He finds too, that commonly there is a rough inverse relationship between the mucus content and gastric acidity.

LYON, BARTLE & ELLINSON (20), have differentiated between a small deposit of mucus sometimes found, which floats on the top of the specimen, and which they consider represents freshly swallowed mucus, and a type of very viscid stringy intimately mixed mucus, which is usually associated with the absence of Free HCl at that particular period of the digestive phase.

It is my experience that not infrequently there/

there is a plug of mucus at the top of the tubes, and that when this has been removed the sample shows commonly no further evidence of mucus

VI. BLOOD.

When the gruel test meal is employed the colour of the samples allow the presence of blood in any quantity to be detected readily by the naked eye.

Its presence may be observed in several forms.

It is not infrequently present as minute flecks in one or two of the samples from a test. It seems probable that blood in this form is due to trauma during intubation (BENNETT (51)).

And therefore too much importance should not be attached to finding occult blood in the gastric samples, or even in the resting content. Blood from this source may easily escape detection by the naked eye, and yet be sufficient in quantity to produce a reaction to a delicate occult blood test.

It was partially with a view to minimising trauma that RYLE (53), introduced his modification of REHFUSS'/

REHFUSS' tube. I have been unable to find any reference to the comparative success of his modification from this point of view, and personally I have had no experience of REHFUSS' tube.

I find, however, that a few flecks of blood are still found in very many cases when RYLE'S tube is used. On several occasions I have tested the stools following the test, for occult blood, in cases in which blood of this degree had been found in the test specimens, but in no instance has an occult blood reaction been given in these cases.

This is in accordance with ABRAHAMS (54) observation that fully 1 c.c. of blood is needed before it can be found in the stools by the most delicate tests.

Blood from sources other than the stomach may be swallowed into it, and LERMANN, REHFUSS & HAWK (52) describe that in such cases the blood found in the samples will be small in amount, discrete, aerated and floating on the surface of the specimen.

Blood may also be found diffused through the specimens, staining them throughout. In which case a local cause, such as carcinoma or ulcer seems most/

most probable.

Though LYON, BARTLE & ELLINSON (20), suggest that even fair quantities of blood throughout the samples should be interpreted more often as being due to mucosal congestion with diapedesis, or to miliary erosions.

While "coffee ground" material may be removed with the resting contents and can be recognised readily.

VII. THE RESTING CONTENT.

THE RESIDUE AT TWO HOURS, AND the GENERAL APPEARANCE of the SAMPLES.

That the amount of resting juice is subject to wide variations in health, both in different persons, and in the same person on different occasions has been referred to already.

Various estimations have been made of the average normal amount of the resting content.

REHFUSS, BERGHEIM & HAWK (55), consider 30 - 180 c.c. to lie within normal limits, but more recently/

recently LERMANN, REHFUSS & HAWK (52), find 20 - 100 c.c. a better approximation to the average.

While CARLSON (3), found variations from 5 - 120 c.c. in these fistula cases in several hundred observations,

The cause of the resting content and these extreme variations in quantity, has not been explained satisfactorily.

That gastric secretion is a continuous process is well recognised and that the rate of secretion of this continuous gastric discharge, varies from time to time in each individual , has been shown clearly.

CARLSON (3), finds reason to suggest that these extreme variations in the resting content are related to alterations in gastric tonus and motility rather than to alterations in the rate of the continuous secretion.

LOEFER (56), finds that there is an increased molecular concentration of the residue in the stomach, and that this favours pylorospasm, and hence further retention.

SOKOLOW (57), has shown that saliva, bile, and pancreatic juice are all capable of stimulating gastric/

gastric secretion. This suggests their presence in the stomach may account for part of the resting content.

FOWLER & ZENTMIRE (42), find that resting juice is in part the result of the activity of the gastric glands and in part the result of fluid, which passes, by osmosis, through the walls of the stomach into the lumen, while duodenal regurgitations, saliva, and oesophageal secretions all play a part.

Finding that the gruel meal had sometimes disappeared before the stomach was completely empty, BENNETT & RYLE (15), remark that just as the stomach before the meal contains juice, so does a certain amount of secretion continue after the meal has passed on.

So that it is difficult to arrive at any satisfactory figure for the quantity for either the resting juice or the residue in normal cases. It may be said, however, that the quantity of content at these times is not of such great significance apart from the composition, and it is only in the absence of evidence of stagnation in the resting content, and of gruel meal in the residue, that a large quantity

of fluid at the beginning and the end of the test, is suggestive of excessive secretion.

With regard to the acidity of the resting contents it may be noted that marked differences between the Free Acid and Total Acidity, are considered to be suggestive of the presence of a relatively high concentration of acids, e.g. lactic acid, other than hydrochloric.

It would appear that the value of microscopical examination of the resting contents, is somewhat doubtful. Certainly none of the tests suggested for the diagnosis of cancer, which depend upon the recognition of unusual substances in the contents are of any value (BENNETT (51)).

Pus cells may be found microscopally, but LERMANN, REHFUSS & HAWK (52), consider that in about 98% of cases in which pus is found in the stomach the focus is extra gastric.

GANZ (58), has shown that it is important to compare the cell count of the sputum with that of the gastric fasting juice, before pus can be accepted as of gastric origin.

While microscopical examination for food residue/

residue may only show that delay in emptying is even greater than demonstrated by charcoal.

The foul odour of the resting juice may in some cases afford confirmatory evidence of stagnation.

The presence of bile, mucus, and blood in the specimens has been referred to already, and the significance to be attached to the appearance of the samples, apart from these, seems uncertain.

All variations in appearance of the samples are found, from these showing a clear supernatant fluid and clear deposit to those in which the whole sample has a dirty gray appearance, and the secretion and deposit are apparently intermingled in mucus.

It is my impression that the appearance bears a definite relationship to the amount of mucus present.

THE/

THE FEATURES OF THE FRACTIONAL ANALYSIS CHART.

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THE VIEWS which CERTAIN AUTHORITIES have expressed in regard to the PRACTICAL VALUE of the FRACTIONAL METHOD of GASTRIC ANALYSIS.

I have thought it might not be without interest to record at this stage before I pass on to a consideration of the results obtained in my series of cases, the views which certain authorities have expressed upon the practical value to be attached to the fractional method of gastric analysis.

I have chosen five such authorities, and these five men have been chosen quite apart from the nature of their views upon this question, but rather as representing different schools of thought from which the test may be viewed.

This group of authorities includes a physiologist, a surgeon, a physician whose name is closely associated with the development of the test in this country, a physician who may view the test in the light of many years astute clinical observation covering all branches of medicine, and an American physician who has devoted considerable study to the test, LIM (1), writes:-

"The only information of value which the test meal does afford is on emptying/

emptying time and retention (as furnished by the presence of a peak or plateau in the gastric secretory curve plotted from fractional observations), so that routine test meal examination can hardly be regarded as a gastric secretory test at all.

It is questionable whether any method of gastric analysis serves a useful purpose in the diagnosis of gastric disorders, excepting perhaps in the observation of the basal or unstimulated secretion. ..... one cannot but feel therefore, that the practitioner will lose nothing by continuing to rely upon those evidences for his diagnosis, and that he will supplement these with radiological examination when he wishes information on pyloric tone or motility.

On the other hand gastric analysis still remains an important method, both for the clinical teacher and investigator".

SHERREN (2), writes:-

I am still of the opinion that for diagnostic purposes the single test meal, before and after operation, gives all the information/

information necessary, and certainly in hospital work it has given me results which correspond more closely to the clinical and operation findings than the fractional".

He then quotes a case in which an unconvincing result was obtained by the fractional method of gastric analysis in view of the operation findings, and continues:-

"In a long experience of EWALD test meals in chronic duodenal ulcer, I have never had a result of this sort, but I have had similar very puzzling discrepancies with the fractional meal. I have abandoned examination by this method except in an endeavour to throw light on exceptionally difficult cases".

RYLE (3), writes:-

"In summary we may conclude that the practical utility of the fractional method has been sufficiently established; its value in clinical work, as will be shown, is great, but it cannot be regarded as a"diagnostic" test excepting in the presence of obstructive lesions".

HUTCHISON (4), writes:-

"In/

"In ordinary practice I consider that the old "single" or EWALD test meal, is to be preferred to the more modern "fractional" type, as the latter is too time consuming, and in the great majority of cases the single meal gives all the information one wants, especially if one supplements that information by a study of the contents obtained from the fasting stomach".

WHEELON (5), at the conclusion of an article criticising the fractional method of gastric analysis on the grounds that the stomach contents are not homogeneously mixed, writes:-

"The correlation of all data is essential to succesful interpretation of gastric curves. I confirm GREEN'S (6), observation. The use of roentgenary and exploratory incision has displaced the systematic examination of gastric contents to an unjustifiable degree. In relation to the stomach, the tube is the most valuable of our aids to diagnosis and therapy".

Consideration of the quotations above shows how widely opinions differ in regard to the practical/

practical utility of the fractional method of gastric analysis, and this suggests a variability in the results obtained by this method, which calls for fuller investigation.

Naturally comparisons are made frequently between the value of the "one hour" test meal and the fractional method of gastric analysis. Since my thesis is concerned primarily with the constancy of the finsings by fractional analysis, it is interesting to record the only reference to the constancy of findings by the "one hour" test, which I have been able to discover.

LEVINE who has carried out a prolonged investigation upon the constancy of the "one Hour" test meal writes:-

> "I conclude that a series of at least three gastric analysis of the same type shall be performed on successive days, and the constancy of the percentage relationship of the titratable factors should be determined before any conclusion or opinion is formed".

It would appear therefore, that the "one hour" test meal is subject to considerable variation in/

in the same individual. That the same may be said of the fractional method of gastric analysis, will be shown in the section which now follows.

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ANALYSIS of the FEATURES of CHARTS obtained from CONSECUTIVE TESTS in seventy five cases presenting GASTRIC SYMPTOMS.

Having considered the factors which may possibly account for daily variations in the results of fractional analysis in some detail, I am now considering the actial variations, which have been found in my series of cases.

Each feature of the chart is again dealt with separately, and the variations found in each point, are recorded in various ways and discussed.

In certain instances I have endeavoured to establish a relationship between variations in one point and variations in some other point.

It has been my endeavour throughout to obtain information which will be of some practical value in the interpretation of the results of fractional analysis, and in determining the manner in which the results of this investigation were to be recorded. I have had this purpose ever in view.

It is clear that a test of this nature would become of little practical value if accurate information is gained only by frequent repetition of the test in any//

any one case. I have therefore, studied the direction of variation, between a first test and a subsequent test of all features in some detail, so that indication may be given of the results which are to be obtained from a second test as compared with a first test, without the necessity of a second test actually being performed.

In determining the method by which variations were to be gauged and recorded, I have experienced considerable difficulty, particularly in respect of the acid curves.

Reference to the work of others in this respect has not proved helpful.

BELL & McADAM (1), from the single case which they investigated devised complicated tables of "standard deviation and coefficient of variation".

While KOPELOFF (2), avoids figures and uses broadly discriptive terms in regard to the variations which he found in thirty normal persons, e.g. "Curves from the same individual vary as much from another, as the differences between the curves of different individuals. While variations in the highest point on curves/

curves from the same individual often exceed differences between the highest points of different individuals".

The importance of finding some practical mode of expressing what may be considered average normal daily variations has increased at the present time, since there is a tendency to develop the use of fractional analysis as an indication of progress following treatment e.g. following gastro-enterostomy.

Reduction of acidity, as estimated by test meals, should therefore, only be recorded as such, provided it exceeds average normal variation.

I have indicated the points with which I am more directly concerned in this thesis, and it is no part of my purpose to enter into any question as to the diagnostic importance to be attached to fractional analysis.

I should like to make it clear, however, that the cases dealt with in this investigation, are of a type in which the test is usually employed.

A great deal of the work upon fractional analysis in this country has emanated from Guy's Hospital, and I have found it desirable, to employ in this/

this thesis the classification of "dyspepsias" which is most frequently used in conjuction with fractional analysis in that school.

CLASSIFICATION of the DYSPEPSIAS.

GROUP 1. HABIT DYSPEPSIAS.

Dyspepsias resulting from faulty physical habits.

Examples: Overeating, under-eating, over work, lack of occupation and exercise, insufficient mastication, constipation, or some combination of these factors.

GROUP 2. NERVOUS or PHYSCHOGENIC DYSPEPSIAS.

Dyspepsias due to faulty mental, or nervous adjustment.

Examples: Nervous tricks, such as, aerophagy, nervous exhaustion, worry, anxiety states, hysteria hypochondriasis, and refusal of food.

GROUP 3. TOXIC and INFECTIVE DYSPEPSIAS.

Dyspepsias due to:-

(a) tissue poison.

(b) general and local infective disease, and other/

other and more obscure conditions interfering with general health and nutrition.

Examples:

(a) Alcohol and Tobacco.

(b) Pulmonary tuberculosis, oral sepsis, severe anaemias, states of general debility associated with auto-intoxication, muscular hypotonus, loss of fatty deposits and visceroptosis.

GROUP 4. IRRITATIVE DYSPEPSIAS.

Dyspepsias due to stimuli originating in a local or distal organic lesion.

Examples: Gastric and Duodenal ulcer, gastro-jejunal ulcer, chronic infections of the appendix, and gall bladder, special sense disturbances, such as astigmatism and central nervous lesions, such as tabes dorsalis.

GROUP 5. MECHANICAL DYSPEPSIAS.

Dyspepsias due to gross structural disease or to surgical modifications of the anatomy of the stomach.

Examples/

Examples: Pyloric stenosis, hour glass stomach, chronic extensive ulceration, certain modifications and sequelae of gastro-jejunostomy, and carcinoma ventriculi.
(quoted from RYLE (3))

It is clear that with any such classification there is considerable overlapping of the different groups, and the exact grouping of cases according to the above classification will vary with each individual observer.

RYLE (3), gives the distribution of these groups, from the investigation of a large series of cases, as follows:-

Group 1.	(Habit Dyspepsias)	12 per cent
Group 2.	(Nervous Dyspepsias)	24 per cent
Group 3.	(Toxic and Infective Dyspepsias)	12 per cent
Group 4 & 5.	(combined) (Irrititative and Mechanical Dyspepsias).	52 per cent

When my series of seventy five cases are grouped according to this classification the following result is obtained:-

Group 1.	15 per cent	(Cases I - XIII)
Group 2.	11 per cent	(Cases XIV - XXI)

Group/

Group 3. 26 percent (Cases XXII - XL)

Groups 4 & 5 42 per cent (Cases XL - LXXV)

It will be seen from comparison of the grouping of my cases with that of RYLE in a more extensive series, that this investigation has been carried out in cases, which may be considered fairly as representing the general run of gastric symptoms of all kinds.

For the sake of convenience I have presented the case records in which the final diagnosis arrived at will be found, together with the actual charts obtained from these cases, in the form of an appendix.

In the present section an analysis of the results of my investigation into the variability of "fractional test meals" is given,

INTERVAL/

INTERVAL between the TESTS.

The following table TABLE III, shows the number of days which elapsed between the first and the second "test meal" in this series of seventy five cases.

TABLE III.

INTERVAL in DAYS	NUMBER of CASES	PERCENTAGE
ONE	35	46.6
TWO	31	41.3
THREE	5	6.6
FOUR	4	5.3

It will be noticed from this table that 88 per cent were re-examined within two days or forty eight hours of the first test, and that the average interval which elapsed between the tests was only 1.7 days or about forty hours.

In the 12 per cent of cases in which the interval between tests exceeded two days, no active treatment was employed, and every effort was made to maintain/

maintain the circumstances of the patient in an unchanged state relative to the first test.

In no case did the interval exceed four days.

THE/

THE BEHAVIOUR of the PATIENT towards the TESTS.

It is difficult to assess this factor in each case, and an arbitrary classification only can be adopted. Further classification of cases in this respect must depend largely on a personal factor in the observer.

I have thought it most satisfactory to use as my index for this purpose, the way in which the patient swallowed the tube.

Only a rough indication of the terms I have employed can be given.

I have considered "easy" those cases in which the patient carefully followed out the instructions for swallowing the tube, and in which the performance was carried through in a deliberate and determined manner.

"Difficult" cases are those in which the patient, having failed to swallow the tube at the first attempt, became excited, and failed to pay attention to the instructions given, until calmed again.

"Very Difficult" cases include those in which/

which some retching is produced, and who are obviously alarmed and distressed by the process.

"Stilette used" indicates patients of the "very difficult" group who were tested after I had devised the stilette to which I have referred already. But I have tended, towards the end of this investigation, to use the stilette in case of the "Difficult" group as well.

TABLE IV.

TEST.	WAY TUBE TAKE.	NUMBER of CASES	PERCENTAGE.
1st	"Easy"	46	61.3
	"Difficult"	14	18.6
TEST.	"Very Difficult"	4	5.3
	"Stilette used"	11	14.6
2nd	"Easy"	65	86.6
	"Difficult"	9	12.0
TEST.	"Very Difficult"	1	1.3

Of these seventy five cases two were known/

known to have had "one hour" test meals on previous occasions: and both these patients are found in the "easy" group in TABLE IV. In no case did any patient who had once swallowed the tube "easily" have any "difficulty" on the occasion of the subsequent test.

It will be noticed from this table that the "easy" group had increased to 86 per cent for the second tests, as against 61 per cent for the first tests.

In this connection the following point may be worthy of note.

Out of 18 cases which were "Difficult" or "Very Difficult" in 1st Test, 38.8 per cent remained "Difficult" or "Very Difficult" in 2nd Test.

Out of 11 cases in which the stilette was used in 1st Test (cases potentially "Very Difficult") only 27.3 per cent were "Difficult" in the 2nd Test, the remainder being "Easy", and in no case was the stilette used in a 2nd Test.

This result would seem to indicate that some value attaches to the use of the stilette, particularly if a second test is contemplated. The numbers are clearly too small for any definite assumption/

assumption to be made.

In my series of seventy five cases, thirty nine have been males, and thirty six, females, so that the slight difference between the numbers according to sex allows fairly accurate study of sex variations from this series.

The present investigation is of some interest in regard to sex in relation to the behaviour of the patient towards the tests. (see TABLE V).

TABLE V.

TEST	WAY TUBE TAKEN	NUMBER OF CASES		PERCENTAGE	
		MALE	FEMALE	MALE	FEMALE
1st	"Easy"	29	17	74.3	47.2
	"Difficult"	3	11	7.7	30.5
TEST.	"Very Difficult"	3	1	7.7	2.7
	"Stilette used"	4	7	12.8	19.5
2nd	"Easy"	37	28	95.0	77.7
	"Difficult"	1	8	2.5	22.3
TEST.	"Very Difficult"	1	—	2.5	—

It/

It is noteworthy that 95 per cent of males have taken the tube easily for the 2nd test, but that 22 per cent of females still have some difficulty in the 2nd test.

THE/

THE CONSTANCY of the TYPE of CURVE.

Of the various classifications which are used in describing the type of curve obtained by fractional analysis, those which are most outstanding are the REHFUSS classification, and the Guy's Hospital classification.

The former is described by MACLEAN (4), as follows:-

"The normal type of curve in which there is a definite rise ending in a peak or short plateau and followed by a more or less steep fall, is known as the ISOSECRETORY curve.

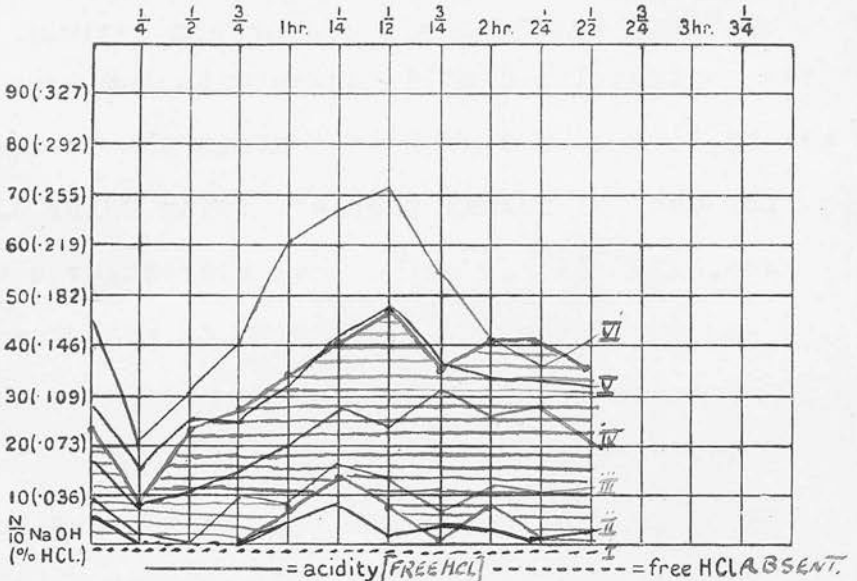
"When the curve is distinctly higher than in the isosecretory form, it is generally referred to as the HYPERSECRETORY type.

"The HYPOSECRETORY curve is represented by the form in which the acid concentration remains below the normal during the whole course of the investigation".

Of the latter classification BELL (5), writes:-

"A purely arbitrary method of classification is/

CHART XX.



The shades area represents the limits of free HCl in 80 per cent of normal persons.

The method of classification of curves adopted as illustrated by average examples of each, i, ii, iii, etc., refer to the types as detailed in the text.

[Bell]

is adopted, based upon a comparison between the free hydrochloric acid curves with the area plotted by BENNETT and RYLE to contain the curves of 80 per cent of normal people". (vide CHART XX).

I. ACHLORHYDRIA, in which free hydrochloric acid, as determined by dimethylamido azobenzene indicator, is present at no period of the analysis.

II. HYPOCHLORHYDRIA, in which the curve has not exceeded the 10 unit (0.036 per cent HCl) line.

III. LOW NORMAL in which the curve follows the lower limit of the 80 per cent normal area.

IV. NORMAL, corresponding to the central zone in which BENNETT and RYLE found 50 per cent of the curves of normal people.

V. HIGH NORMAL, in which the curves approximate to the upper limit of the 80 per cent normal area, and even exceed it somewhat.

VI. HYPERCHLORHYDRIA, in none of which is free HCl lower than 60 units (0.219 per cent HCl) at one or more periods of the analysis.

Of these two classifications I have adopted this latter as being more suitable for my present purpose/

High Normal	High Normal	5	3	2	4	1
High Normal	Hypochlorhydria	1	1	-	-	1
High Normal	Normal	5	4	1	1	1
High Normal	Hyperchlorhydria	3	2	1	3	-
Hyperchlorhydria	Hyperchlorhydria	5	5	-	5	-
Hyperchlorhydria	Low Normal	1	-	1	1	-
Hyperchlorhydria	High Normal	3	2	1	-	1
Irregular	Low Normal	1	1	-	-	-
Irregular	Normal	2	1	1	-	2

Type of Curve the same in 1st and 2nd Test 40 cases = 52.6%
Type of Curve differed in 1st and 2nd Test 35 cases = 47.4%

TABLE VI.

TYPE OF CURVE IN 1ST TEST	TYPE OF CURVE IN 2ND TEST	NUMBER OF CASES IN RELATION TO TYPES OF CURVE	MALE	FEMALE	THE BEHAVIOUR OF THE PATIENT TOWARDS THE TESTS	
					EASY IN BOTH TESTS	DIFFICULT IN 1st TEST. EASY IN 2ND.
Achlorhydria	Achlorhydria	16	6	10	5	4
Achlorhydria	Hypochlorhydria	2	-	2	1	1
Achlorhydria	Low Normal	2	-	2	1	-
Hypochlorhydria	Hypochlorhydria	3	1	2	2	-
Hypochlorhydria	Low Normal	3	2	1	2	1
Hypochlorhydria	Normal	1	-	1	1	-
Low Normal	Low Normal	4	2	2	3	1
Low Normal	Achlorhydria	1	1	-	1	-
Low Normal	Hypochlorhydria	1	1	-	1	-
Low Normal	Normal	2	1	1	1	-
Normal	Normal	7	4	3	4	3
Normal	Achlorhydria	1	-	1	1	-
Normal	Low Normal	4	-	4	-	1
Normal	High Normal	2	2	-	1	1

purpose, since it allows a finer degree of comparison of the curve from the first test with that from the second test.

I have found it desirable to add to this classification the term IRREGULAR: as I found three cases in which the curve from the first test could not be fitted into any of the groups. These"irregular" curves have consisted in a relatively high percentage of free HCl making a delayed appearance after the end of one hour.

In the TABLE VI the cases are grouped according to the type of curve found in the first test. These groups have then been compared with the type of curve found in the second test in each case. In this way variations between the type of curve obtained by the two tests is shown, and from a study of this table the important fact is shown, that of seventy five cases examined, in forty cases the type of curve (as estimated according to the classification employed) remained the same, but that in thirty cases the type of curve varied. It would appear therefore, that in almost 50 per cent of cases the type of curve is subject to variations.

The number of cases in each group is too small/

small to allow of the comparisons being made, but it is noteworthy that, while 50 per cent of cases showed variations in the type of curve in the Low Normal & Normal groups &almost 50 per cent in the Hyperchlorydria group, the High Normal group showed that 66 per cent of cases in that group were subject to variation.

In regard to the small percentage of variations namely 20 per cent, in the Achlorhydria group it may be said that this classification clearly allows this group to cover a wide range of curves between achylia and hypochlorhydria, and that the smallest percentage variations is to be expected in this group.

It was considered possible that either a sex factor or the behaviour of the patient towards the test might play a part in the production of variations in the type of curve in any case. Attention has therefore been paid to these points in the table shown (TABLE VII). In this way it is seen that neither sex nor the behaviour of the patient towards the test seem to play any part in determining variations in the type of curve.

TABLE/

TABLE VII.

	WHOLE SERIES.		MALES.		FEMALES.		THE BEHAVIOUR of the PATIENT towards the TEST.			
	Number of cases	per cent	Number of cases.	per cent	Number of cases	per cent	"EASY" in both tests.		"DIFFICULT" in 1st Test "EASY" in 2nd Test.	
							Number of cases	per cent	Number of cases	per cent.
TYPE of CURVE similar in 1st and 2nd TESTS.	40	52.6%	21	56.4%	19	52.8%	23	47.9%	9	50%
TYPE of CURVE differed in 1st and 2nd TESTS.	35	47.4%	18	43.6%	17	47.2%	15	52.1%	9	50%

It will be observed that the percentage variation in the type of curve remains relatively unchanged whether considered for the whole series, or according to sex, or in relation to the behaviour of the patient towards the test.

Clearly the classification employed is to a large extent arbitrary, and it allows a personal element to enter into the grouping of certain curves. I would note here that whenever I was in doubt as to the exact grouping of a curve from a second test, I have favoured the grouping which approximated most nearly to the first curve.

So that, if anything, the percentage variations in the type of curve as shown, errs on the small side.

NOTE.

The results which I have obtained show clearly that this method of classification is unsatisfactory.

It is of some interest to note, therefore, that since this paragraph was written KOHIYAR has recorded a comprehensive survey of 1080 cases, examined by fractional analysis, either at Guy's Hospital or New Lodge Clinic, which is based entirely on this mode of classification.

KOHIYAR - Guy's Hospital Reports, 76 1926.

THE AVERAGE DIFFERENCE in all the fractional samples from CONSECUTIVE TESTS in any one case in terms of cubic centimetres of $\frac{N}{10}$ NaOH per 100 cubic centimetres of gastric contents.

Since it has been shown in the last section that in nearly 50 per cent of cases there is a variation in the type of curve, when attempts are made to classify the curves according to existing nomenclature, it seems desirable to study the variations by some numerical standard.

For this purpose the difference between the same sample in the 1st. and 2nd. test respectively, has been estimated in respect of both free HCl and Total acidity in every case. In this way the average difference over all the fractional samples, has been found in each case.

The unit of difference employed has been cubic centimetres of $\frac{N}{10}$ NaOH per 100 cubic centimetres of gastric contents.

In compiling this average difference of samples in each case, the resting content of the stomach has not been considered, and the average difference in the contents removed before the test meal was given, will be dealt with later.

The/

The resting content has been omitted with a view of obtaining more standard results, for clearly the constitution of this particular sample depends upon factors which cannot be controlled adequately.

TABLE VIII. shows the average difference found in my seventy five cases estimated in the way I have indicated.

TABLE/

TABLE VIII.

DIFFERENCE between CURVES of 1st & 2nd TESTS in c.c. of $\frac{N}{10}$ NaOH per 100 c.c.	WHOLE SERIES		MALE		FEMALE	
	FREE HCl 60 CASES	TOTAL ACIDITY 75 CASES	FREE HCl 36 CASES	TOTAL ACIDITY 39 CASES	FREE HCl 24 CASES	TOTAL ACIDITY 36 CASES
AVERAGE	11.6	9.7	12.2	11.6	11.5	8.1
MAXIMUM	31.8	31.5	31.8	24.2	28.5	31.5
MINIMUM	4.0	2.2	4.0	2.2	4.2	2.2

It will be seen that in all cases there is on the average a difference of 11.6 units of Free HCl and 9.7 units of Total Acidity, between similar samples from consecutive tests.

This average difference far exceeds the two or three units which WHITE (7), considered attributable to experimental error, and which as I mentioned in the last section, I found occasionally in re-testing certain samples.

Sex appears to play no part in accounting for this difference.

It has seemed advisable to consider this difference in relation to the behaviour of the patient towards the test.

TABLE IX.

BEHAVIOUR of PATIENT TOWARDS TESTS	AVERAGE DIFFERENCE FREE HCl	AVERAGE DIFFERENCE TOTAL ACIDITY
"EASY" in BOTH TESTS	11.2	10.8
"DIFFICULT" in 1st TEST "EASY in 2nd TEST	11.6	11.6
WHOLE SERIES IRRESPECTIVE of BEHAVIOUR	11.6	9.7

It would appear that this factor does not influence the average difference in any way, for the average figures obtained in cases considered from this point of view are entirely comparable with those obtained from the whole series, and the difference between cases in which the tube was swallowed "easily", and those in which "difficulty" was experienced in the first test is negligible as regards Free HCl.

It will be noticed, however, that in cases in which there was "difficulty" in swallowing the tube during the first test the average difference in Total Acidity is definitely in excess of that found in the whole series.

The following observation would seem to have some bearing on this point.

There were in all forty six patients who swallowed the tube "easily" at both 1st and 2nd tests, and nineteen who had "difficulty" in the 1st test but were "easy" in the 2nd.

Of these forty six easy patients 10.8 per cent were noted as having mucus in the 1st test only, while of the nineteen "difficult" cases 31.6 had mucus in the 1st test only.

It/

It would seem therefore that there is a greater frequency of mucus in cases in which the tube is swallowed with "difficulty".

BENNETT & RYLE (6), have observed that in cases in which there is an abundant secretion of mucus, the average difference between the parallel curves of Free and Total acidity is greater than usual.

The relative increase of mucus with "difficult" cases, along with an increase of titratable total acidity, associated with the presence of mucus is therefore, sufficient to account for the average difference of total acidity in "difficult" cases being, as I have recorded above the normal for my series of cases, while the average difference in Free HCl in "difficult" cases, remains within normal limits.

In studying the curves from my cases I have observed that actual average variation, as measured in units appears to differ according to the type of curve, when the curves are classified in the way I have described.

This is illustrated in the following TABLE X.

TABLE/

TABLE X.

CASES which showed VARIATION in the TYPE of CURVE classified according to TYPE of CURVE from 1st TEST.	AVERAGE DIFFERENCE	
	FREE HCl	TOTAL ACIDITY
ACHLORHYDRIA	11.0	8.9
HYPOCHLORHYDRIA	9.0	8.3
LOW NORMAL	5.3	6.7
NORMAL	9.4	9.1
HIGH NORMAL	13.7	11.7
HYPERCHLORHYDRIA	16.6	17.6
IRREGULAR	15.3	13.4
Whole SERIES irrespective of ALTERATION in TYPE of CURVE	11.6	9.7

It will be seen that the average difference is relatively smallest in the case of curves of the "Low Normal" type, and that in the groups both above and below this type, the average difference increases steadily.

It/

It seems probable that the explanation of this observation lies in an inequality which the arbitrary method of classifying the curves according to type allows, so that relatively slight alterations only in the acidities in consecutive tests are required to displace "Low Normal" curves from that group, while greater difference in acidity is needed before the type becomes altered in the case of other groups, particularly the higher ones e.g. "High Normal" and "Hyperchlorhydria".

This explanation seems desirable lest it be thought that the results I have recorded suggest that cases with "Low Normal" curves are relatively much more consistent than those whose curves lie in other groups.

THE/

THE AVERAGE DIFFERENCE in the FRACTIONAL SAMPLES in relation to the TIME PERIOD of each sample.

Having observed the average difference between all the consecutive test samples as a whole, it is desirable to consider the average difference of consecutive samples withdrawn at the same time period.

By this means it may be seen at what time period during the two hours of the test the curves of acidity most nearly approximate to one another.

TABLE/

TABLE XI A. (Free HCl)

TIME PERIOD	Resting Content	¼ HR.	½ HR.	¾ HR.	1 HR.	1¼ HR.	1½ HR.	1¾ HR.	2 HR.
HYPOCHLOR-HYDRIA.	4	7	9.7	14	10.4	13.1	12.3	10.5	7.8
LOW NORMAL	8.6	5.2	8.1	7.8	11	9.1	7.5	8.5	7.7
NORMAL	13.8	2.6	9.7	12.1	1.3	13	9.5	11.6	10.2
HIGH NORMAL	18.6	8.8	10.5	16.6	16.3	15.5	13.7	15.4	17.4
HYPERCHLOR-HYDRIA.	21.6	8.7	13.6	19	19	17.5	12.7	16	26
AVERAGE of whole SERIES excluding ACHLOR-HYDRIA.	15.9	6.9	10.4	13	13.9	13.6	11.1	12.4	14.7
ACHLOR-HYDRIA. (only three cases showing Free HCl in 2nd Test)	0	20	13	11	12.5	10.6	8	0	0

TABLE XI B. (Total Acidity)

TIME PERIOD	Resting Content.	¼ HR.	½ HR.	¾ HR.	1 HR.	1¼ HR.	1½ HR.	1¾ HR.	2 HR.
HYPOCHLOR-HYDRIA.	14.6	6.6	6.8	7.1	10.6	9.4	11.7	7.7	8
LOW NORMAL.	5.9	5.5	6.6	8.2	9.1	6.8	4.4	7.9	7.3
NORMAL	14.2	5.5	5	9.4	12.5	12.3	8.7	9.4	9
HIGH NORMAL	19.3	7.2	12.3	14.7	15.2	13.5	13.1	13.4	20.4
HYPERCHLOR-HYDRIA	18.6	10	17.4	16.9	19.3	17.7	14.2	11.2	27.5
AVERAGE of whole series except ACHLOR-HYDRIA.	14.5	6.9	9.6	11.2	13.3	11.9	10.4	10.9	14.4
ACHLOR-HYDRIA.	12	4.9	5.6	5.8	5.6	5	3.5	4.6	4
AVERAGE of whole SERIES including ACHLOR-HYDRIA.	13.1	6.6	8.6	10.3	12	10.8	9.1	9.9	9.9

TABLES XI A & B have been arranged to show the average difference at different time periods during the test in relation to Free HCl and Total Acidity. These show average differences as computed from the whole series, and also in relation to the different types of curve obtained in the first test. It seemed desirable to consider "Achlorhydria" separately for reasons which I have already given.

It will be noticed that in the whole series the average difference in regard to Free HCl, appeared lowest at a period of 1½ hours from the commencement of the test, apart from the first half hour of the test, when relatively small differences would naturally be expected. This has been true for all types of curve except "Hypochlorhydria" in which some irregularity is seen.

The average difference of Total Acidity has run a very similar course throughout the two hour period, and lowest average difference apart from the first half hour, is also found at the one and a half hour period.

Attention may however be drawn to the difference which exists between the Free HCl and Total Acidity/

Acidity of the resting content in this respect.

It will be seen that the average difference of Free HCl increases as the curves are of a higher type while there is considerable irregularity when the Total Acidity is considered from this point of view. I have been unable to explain this divergence between the Free HCl and Total Acidity, and have been unable to relate it to any excess of mucus in the resting content.

I thought that the behaviour of the patient towards the test might possibly affect the secretion so as to alter the time period at which the two tests were most nearly approximated.

The following table (TABLE XII) shows that this has not been the case.

TABLE XII.

Cases in which the 1st Test was "Difficult" and the 2nd Test "Easy".

	¼ HR.	½ HR.	¾ HR.	1 HR.	1¼ HR.	1½ HR.	1¾ HR.	2 HR.
FREE HCl	8	9.6	11.2	14.3	13.0	9.9	15.8	17
TOTAL ACIDITY	5.7	8	10.2	15.4	12.8	9.5	12.3	13.2

It/

It will be seen that the figures obtained from these cases are comparable to those for the whole series, and the time period giving the closest approximation between the two tests has remained unchanged, namely one and a half hours.

THE/

The STRENGTH of the SECRETORY RESPOMSE in relation to 1st and 2nd TESTS.

Reference has been made already to the fact that in my series of cases, I found that the acid curve from the first test usually runs at a higher level than that obtained from the second test.

When the acid response is judged by the maximum height observed in any sample of either test, the following results are obtained.

TABLE XIII.

	ALL CASES	MALES	FEMALES
HIGHEST RESPONSE in 1st TEST.	61.4%	60.6%	62.5%
HIGHEST RESPONSE in 2nd TEST.	38.6%	39.4%	37.5%

Only cases showing Free HCl in one or other test are considered, and the maximum Free HCl registered at any period, has been used as the index.

It/

It will be observed that in about 60% of cases a higher response of acid secretion has been obtained from the 1st Test.

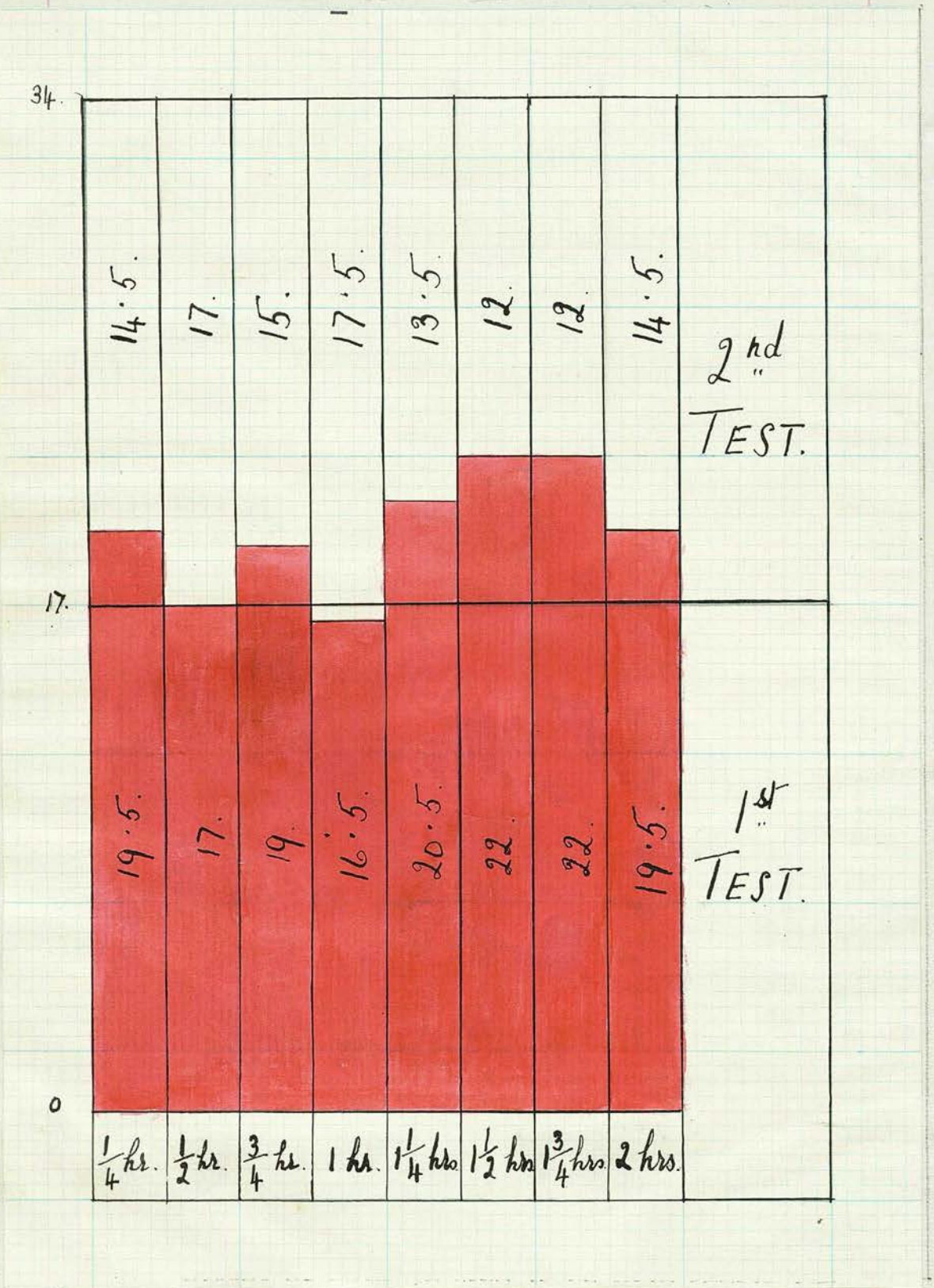
Reference to TABLE VI will show that this is also indicated when the curves are considered according to an arbitrary classification. Thus, of nine cases showing "High Normal" curve in the 1st Test with alteration of the type of curve in the 2nd Test, six cases showed alteration to a lower type of curve, while three were altered to a higher type, and of seven cases showing a "Normal" curve followed by an alteration of the type of curve in the 2nd Test, five cases were altered to curves of a lower type, while in two cases the curves became a higher type.

I have endeavoured to discover whether this higher response from a first test which is usually observed when the curve is considered as a whole, is maintained at the different intervals during the test.

For this purpose I have selected all cases in which the average difference between the curves of Free HCl, from the two tests, was lower than the average difference found for the whole series in this respect. (vide TABLE VIII).

Of/

TABLE XIV.



Showing at each quarter of an hour period the number of times a greater response was obtained from a 1st test, as compared with a 2nd test, in the thirty-four cases selected.

Of such cases there have been thirty four. In these cases I have observed the relationship between the height of the curve from the first test, and the height of the curve from the second test, at each quarter of an hour period.

In TABLE XIV is shown the number of times in in which a greater response was obtained in the 1st test, or 2nd test, at each quarter of an hour period.

It will be observed that a greater number of patients have given a higher acid response at all periods during the ist test, except the half hour and one hour periods. At the half hour period the higher point is seen equally in either 1st or 2nd test, while at the one hour period the chance of the higher point being in the second curve becomes greater than the chance of this point being in the 1st test at this period.

It seemed possible that the behaviour of the patient towards the test might influence this relationship between a higher response and a first test.

I consider these thirty four cases, therefore, from the point of view of "ease" or "difficulty" in swallowing the tube during the first test.

The/

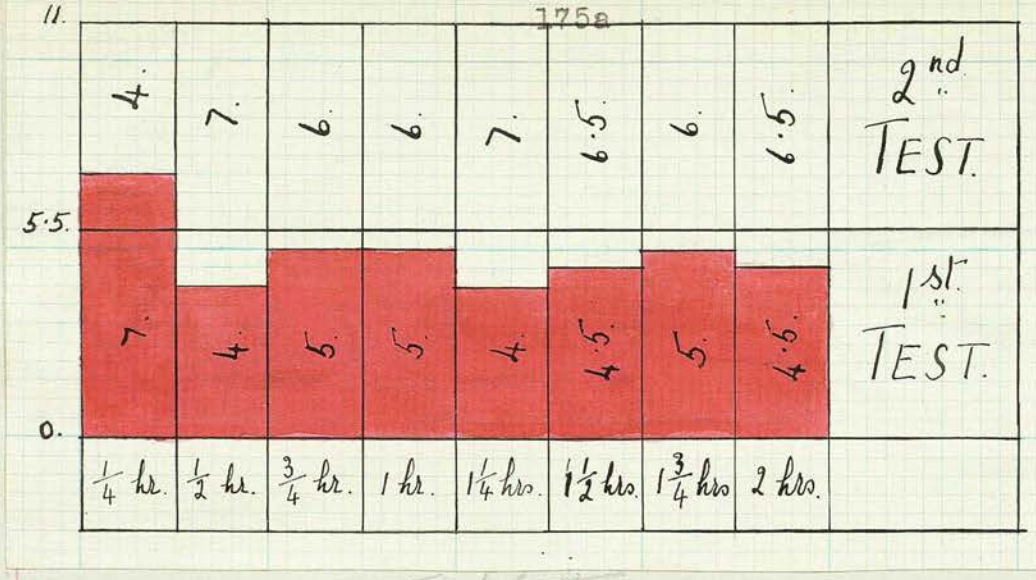


TABLE XV.

Showing the relationship between 1st & 2nd tests in regard to height of response in difficult cases.

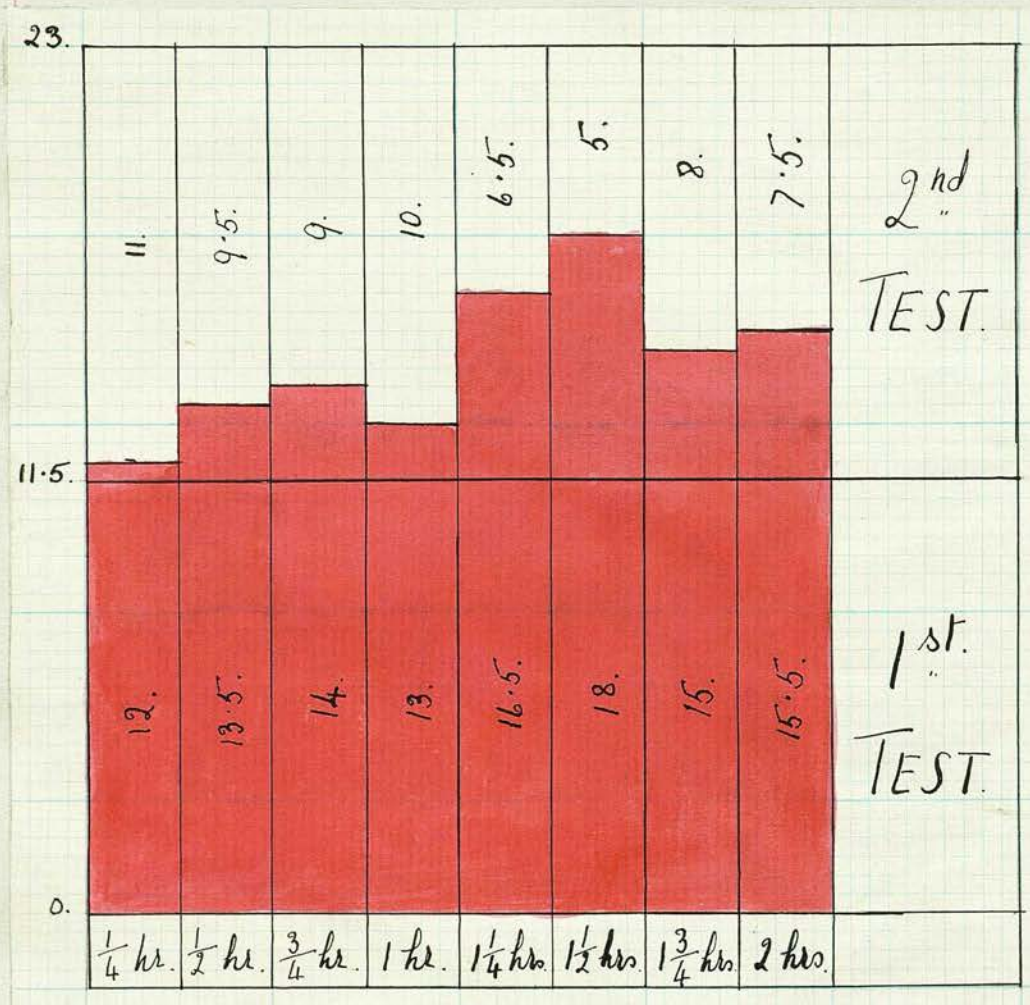


TABLE XVI.

Showing the relationship between 1st and 2nd tests in regard to height of response in Easy cases.

The results obtained when the cases are considered from this point of view are shown in TABLES XV and XVI.

It will be observed that when the "Easy" cases are considered separately, the chances of a higher response being obtained from a first test has increased at all periods, including the half hour and one hour period.

While in the "Difficult" cases the situation has changed completely. In these cases at every period except the first quarter hour, and the one hour and three quarters, the chances of a higher response are greater in the 2nd test.

THE/

TABLE XVII.

CASES SHOWING the last trace of starch in:-	THE SAME SAMPLE ab both tests	42.1%
	SAMPLES which differed by $\frac{1}{4}$ hr.	47.3%
	SAMPLES which differed by $\frac{1}{2}$ hr.	10.5%

Clearly the difference of one $\frac{1}{4}$ hr. period may be considered as of no practical importance since the exact time qt which the last particles of starch leave the stomach is not known, and examination of the samples shows only the presence or absence of starch without indicating how much starch is left in the stomach at any period.

It will be observed, therefore, that in nearly 90 per cent of these thirtyeight cases the rate of emptying was parctically constant.

WHen, however, the thirteen cases, in which starch had left the stomach before two hours in one test, while persisting for two hours in the other test, while persisting for two hours in the other test, are considered in addition, it will be seen that the 90 per cent constancy gives an erroneous/

THE CONSTANCY of the RATE of EMPTYING of THE STOMACH.

The constancy of the rate of emptying of the stomach in any one case as judged by the absence of starch from the samples withdrawn at the later periods of the test is of considerable importance.

This constancy can, of course, be judged with any accuracy only in those cases in which starch was absent before the withdrawal of the two hour, and final sample, in both tests.

Out of my severty five cases there have been thirty eight which can be included in the above category.

Of the remainder, thirteen have shown the presence of starch for two hours, or more at one or other tests. While twenty four have shown starch still to be present in the two hour sample on the occasion of both tests.

In TABLE XVII is shown the results obtained from analysis of the thirty eight cases in which starch was absent before the end of the two hours in both tests.

TABLE/

erroneous impression.

These thirteen cases to which I have referred may be tabulated thus (TABLE XVIII.)

TABLE XVIII.

CASES showing the LAST TRACE of STARCH in samples which differed by:-	¼hr. or more	5
	½hr. or more	4
	¾hr. or more	2
	1hr. or more	2

With a view to determining what is the expectation of constancy in any case in which starch is found by a single test, to have left the stomach before two hours.

I have prepared the following table TABLE XIX) summation of the thirty eight and thirteen to which I have referred.

TABLE/

TABLE XIX.

CASES showing the LAST TRACE of STARCH in:-	The SAME SAMPLE at both TESTS	30.7%	Difference Negligible 65.3%
	SAMPLES which differed by $\frac{1}{4}$hr	34.6%	
	SAMPLES which differed by $\frac{1}{2}$hr	7.7%	
	SAMPLES which differed by $\frac{1}{4}$hr or more	11.7%	
	SAMPLES which differed by $\frac{1}{2}$hr or more	7.7%	Difference possibly of 34.7% importance
	SAMPLES which differed by $\frac{3}{4}$hr or more	3.8%	
	SAMPLES which differed by 1hr or more	3.8%	

It will be seen that while 65 percent of cases show a rate of emptying which remains constant 35 per cent of cases are inconstant in this respect to/

to an extent which may be of some importance.

I have been unable to establish any close relationship between inconstancy of the rate of emptying, and the average difference of acidity from the consecutive tests, in any one case.

The following observation suggests that some relationship of this nature does exist.

It will be recalled that in the whole series of cases the average difference of Total Acidity between consecutive curves amounted to 9.7 c.c. of $\frac{N}{10}$ NaOH per 100 c.c. of gastric contents.

In those cases in which the rate of emptying was found, for practical purposes, to be constant, this average difference of Total Acidity was only 8.5 units. While in four cases in which the rate of emptying was known to have varied by at least three quarters of an hour, this averafe difference amounted to 11.8 units.

NOTES/

NOTES upon MUCUS, BILE, and BLOOD in consecutive TEST MEALS.

MUCUS

I have referred already to the possible association of mucus with the raising of the difference of Total Acidity, disproportionately to the average difference of Free HCl, in cases in which the tube is swallowed with "difficulty".

A further observation has been made which may have some bearing in this connection.

In "Difficult" cases the proportion of Females to Males was 19 to 10.

In cases showing Mucus the proportion of "Difficult" to "Easy" was, 14 to 10.

In cases showing Mucus the proportion of Females to Males was 16 to 10.

Since both the element of "difficulty" and the presence of mucus are hard to assess the proximity of the proportions which I have noted above forms something in the nature of a cross reference, and suggests further the association of "difficulty" with mucus/

TABLE XX.

CASE	1ST TEST	2ND TEST	
II	0	8	
III	not observed	0	
IV	Not observed	0,7,8	
V	0	not observed	
VI	0,5,8	4,7,8	
VIII	8	not observed	
IX	0	0.7.8	
X	0	0	
XIII	0	0	
XIVA	6.7.8	0.4.5.6	0 = Resting Content
XVI	0.7.8	0	
XVII	0.4	0.7.8	1 = $\frac{1}{4}$ hour sample
XVIII	0	78	
XIX	08	not observed	2 = $\frac{1}{2}$ hour sample
XX	08	0	
XXI	0	08	3 = $\frac{3}{4}$ hour sample
XXII	0	078	
XXIII	0678	08	4 = 1 hour sample
XXIV	078	0	
XXV	not observed	0	5 = $1\frac{1}{4}$ hr. sample
XXVI	5678	5678	
XXVII	0678	01678	6 = $1\frac{1}{2}$ hr. sample
XXVIII	0	0	
XXIX	0	0	7 = $1\frac{3}{4}$ hr. sample
XXX	5678	08	
XXXI	04678	0678	8 = 2 hour sample
XXXII	0	0	
XXXIII	78	678	
XXXIV	078	0	
XXXV	01678	01245678	
XXXVI	078	04	

Showing the samples in which Bile was observed in any test in this series.

TABLE XX. (cont.)

CASE	1ST TEST	2ND TEST
XXXVII	0	78
XXXVIII	0	0
XXXIX	not observed	6
XXXIXA	8	0
XLI	not observed	08
XLII	0	78
XLIII	08	04
XLIV	05678	045
XLV	345678	0345678
XLVI	not observed	0
XLVII	8	06
XLVIII	78	not observed
XLIX	not observed	08
L	0	not observed
LI	0678	0345
LII	02345678	023456
LIII	05	0
LV	08	not observed
LVII	08	045678
LVIII	8	not observed
LXIXA	not observed	0
LXII	0	078
LXIII	078	not observed
LXIV	not observed	78
LXV	012345678	05678
LXVIII	not observed	012345678
LXIX	78	05678
LXXII	045	678
LXXIV	12345678	12345678
LIX	012345678	05678
XLIA	0	3

Showing the samples in which Bile was observed in any test in this series.

mucus in this series of cases.

Out of the seventy five cases, thirty four have been noted as showing mucus at some period during one or other test.

Of these thirty four cases, mucus was present in both tests in seventeen, while ten cases have shown mucus in the first test only, and seven have shown mucus in the second test only.

BILE.

The most satisfactory impression of the behavious of bile in relation to the fractional test samples may be gained by examination of TABLE XX.

Of my seventy cases, forty-five have shown the presence of bile at some period during both tests, and in almost 60 per cent of these frankly pathological cases I have found bile present consistently in consecutive tests.

A further eighteen cases have shown bile at some period during one test only, so that in my whole series of cases I have found some indication of duodenal regurgitation in 82.6 per cent.

Consideration of TABLE XX. shows that the sample/

sample in which bile is found with greatest frequency is the resting content, while next in frequency comes the two hour sample, then the one hour and three quarters sample, and so on.

It may be observed that while bile has been found not infrequently in exactly the same samples in both tests, a not uncommon association has been that of bile, in the resting content of one test, with bile in the later specimens only of the other test.

I have referred already to the observation made by BENNETT & RYLE that an artificial reflux of bile may be produced in some instances by suction at the tip of the tube.

I have observed that during suction a syringeful of gastric contents may suddenly be seen to become bile stained occasionally, but I have been unable to estimate either the frequency of this occurence, or the part which it plays as a general rule, in connection with the presence of bile in the gastric samples.

BLOOD.

In the last section I drew attention to the various/

various forms in which blood might be observed in the fractional samples, when estimated microscopically.

In my series of cases blood has been observed in some form during one or other test in thirty three cases. Out of these thirty three cases blood has appeared in the form of flecks only in twenty six.

In the seven remaining cases the blood has appeared in a more gross form, of these five have shown blood in a gross form in samples from both tests, while two showed gross blood in samples from one test only.

It is noteworthy that while these five cases, showing blood in both tests, proved clinically to be cases in which blood might be expected (three gastric carcinoma and two gastric ulcer), the two cases showing gross blood in one test only were clinically conditions in which no blood was to be expected (one gall stones, and one "Habit Dyspepsia").

I have been unable to establish any relationship between the behavious of the patient towards the test and the presence of flecks of blood in the samples.

Of the twenty six cases showing flecks of blood/

blood 60 per cent have been "Easy" patients and 40 per cent "Difficult". These figures being entirely comparable to the 61 per cent "Easy", and 39 per cent "Difficult", which it will be recalled were the figures obtained when the whole series of cases was considered from this point of view.

I have not found any evidence to suggest that the use of the stilette tends to cause more abrasion of the mucus membrane than may be occasioned by swallowing the tube alone.

DIFFERENCE./

DIFFERENCE in the AMOUNT of RESIDUE and RESTING CONTENT from CONSECUTIVE TESTS.

I have not been satisfied entirely that the technique employed has yielded the whole of either the resting content of the residue at every test. I am able to give isolated observations only, upon which this inference has been formed.

For example, in one or two cases I have observed the presence of charcoal in the later samples from a test, despite the fact that every precaution had been taken to remove the entire resting content, and presumably all the charcoal with it, before the meal was given. Further, in several instances, I have been surprised by a sudden withdrawal of either residue or resting content just when suction was about to be abandoned in a view of the failure of preceding attempts at suction to withdraw any contents.

I can, therefore, record the quantitative estimations of contents before and at the conclusion of the test in a tentative manner only.

TABLE/

TABLE XXI

	RESTING CONTENT.	RESIDUE at 2 HRS.
AVERAGE DIFFERENCE between 1st and 2nd TEST.	31 c.c.	19 c.c.
MAXIMUM DIFFERENCE observed in this SERIES.	240 c.c.	200 c.c.
MAXIMUM AMOUNT observed in any CASE.	410 c.c.	320 c.c.
MINIMUM AMOUNT observed in any CASE.	10 c.c.	Nil.

On the whole the figures of 31 c.c. and 19 c,c. for the average difference in Resting Content and Residue respectively, between consecutive tests, give an unfair representation of the results which I have obtained in my cases. A few cases showing very gross differences in amount at the two tests have made the average difference disproportionately high, and it has been my experience that the amounts of both resting content and residue as a rule, vary within much smaller limits than my average figures indicate.

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SUMMARY.

I. Study of the comparative value of various Gastric Secretory and Gastric Motility tests shows that of all the tests which are capable of practical appreciation in these respects at the present time, the Fractional Method of Gastric Analysis is probably the most efficient method of observing either of these functions, and that this test occupies a unique position, in that it is at once, a test of both these functions.

II. Reference to recent advances which have been made in the field of gastric physiology shows that even this fractional test cannot be considered as scientifically efficient, and that it is open to several important, and innumerable minor fallacies.

III. Consideration of the whole principle, and technique of the test (In this thesis I have described, as part of my technique, the use of a form of stilette, such as has not previously been described) in the light of recent physiology/

physiology, of the experiences which certain observers have recorded during the practical application of the test, and of certain incidental observations which I have made in the course of my present investigation, shows that a degree of variation in the results obtained from consecutive tests in the same person, may reasonably be anticipated in a percentage of cases at least.

IV. Investigation into the literature of this subject reveals that only a very limited number of observations have been recorded, concerning the daily variation found by consecutive tests. Such observations as have been made are all concerned with normal persons. No estimation of the daily variation to be found in persons presenting gastric symptoms has, so far as I can ascertain, ever been attempted.

V. I have examined by consecutive tests of a fractional nature, seventy five persons presenting gastric symptoms.

The charts obtained from these consecutive tests are shown in this thesis.

VI. Analysis of the consecutive charts obtained from

from/

from these seventy five cases has led to the following observations:-

(a) Of subjects undergoing the test for the first time about 62 per cent may be expected to swallow the tube easily, and show little or no distress at the circumstances of the test, the remaining 38 per cent may be expected to experience distress or difficulty in swallowing the tube in some degree.

On the occasion of a subsequent test 87 per cent may be expected to swallow the tube easily, and only 13 per cent will present any difficulty.

(b) When attempts are made to classify the acid curves according to an existing nomenclature, the type of curves, obtained by consecutive tests at short intervals of time is found to differ in about 47 per cent of cases.

(c) When the difference between curves, obtained by consecutive tests at short intervals of time, is considered in terms of cubic centimetres/

centimetres of $\frac{N}{10}$ NaOH per 100 cubic centimetres of gastric contents.

I have found that in my series of cases the average difference amounts to 11.6 units in respect of Free HCl, and 9.7 units in respect of Total Acidity.

(d) When the average difference between curves from consecutive tests, is referred to the various quarter of an hour periods, it is found that in respect of both Free and Total Acidity, this average difference is least, apart from the first half hour of the test, at a period of one & a half hrs. following the ingestion of the meal.

That is the curves from consecutive tests approximate most nearly to one another as a general rule, at a period of one and a half hours after the commencement of the test.

(e) In the majority of cases a first test shows on the average, a higher response than a second test. This is true at all the quarter of an hour periods of the test except

at/

at a period of one hour from the commencement of the test, at which period a greater response has, on the average been obtained from the second test.

It has been observed that the way in which the patient swallows the tube influences the results obtained in this respect. For when patients who swallowed the tube easily are considered separately, the number of cases in which a higher response is obtained from a first test increases considerably. While when patients who experienced difficulty in swallowing the tube are considered in a group by themselves it is found that the majority of such patients show a greater response from the second test at which time the tube is usually swallowed with difficulty.

(f) When the constancy of the rate of emptying is estimated by the absence of starch from the later samples of the fractional test meal, it has been found that the rate of emptying remains, for all practical purposes, constant as shown by consecutive tests/

tests, in about 65 per cent of cases. In the remaining 35 per cent of cases there is a variation which may possibly be of some significance.

(g) The presence of Bile, Mucus, Blood and Charcoal (when employed as an adjunct to the technique) in the samples, the amount of resting juice in the stomach and the residue at the end of the test, and the general appearance of the samples are considered as having certain significance.

Considerable variations either in amount or in the time of appearance during the test has been observed, as the result of the examination of samples from consecutive tests, in all these factors.

CONCLUSION/

CONCLUSION.

Subject to the limitations of this investigation (seventy five cases) I am of the opinion that there are considerable variations in the results obtained from consecutive tests, performed at shoet intervals of time, in the same individual, by the fractional method of gastric analysis.

These variations appear to me to be greater then is commonly supposed.

Probably the average amount of variation which I have observed to occur, is insufficient ot affect seriously the diagnostic significance of the results obtained from this test.

In certain cases more extreme variations do occur, and in these cases the interpretation of the results must be to some extent erroneous.

I have been unable to discover any single factor, which played the sole part in the production of such variations as I have observed, and I consider that daily variations will be found, most probably to be the produce of several small differences, each operating/

operating at some different point in the chain of events, which occur between the functioning of the stomach, and the estimation of the results, in the case of each test.

There would seem to be sufficient indication that daily variations in the results obtained from fractional analysis, have not been studidied adequately.

I am, therefore, of the opinion that further investigation is called for, in the study of daily variations in both normal and pathological subjects.